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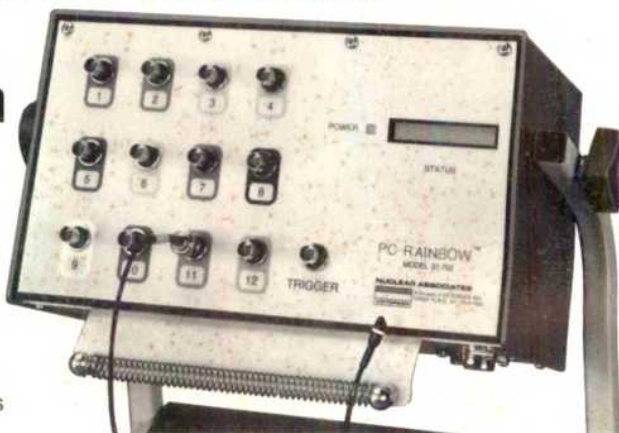
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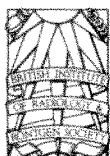
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A quantitative study of lumbar vertebral bone marrow using T_1 mapping and image analysis techniques: methodology and preliminary results

By §N. Roberts, PhD, *S. R. Smith, MRCP, †D. F. Percy, PhD and R. H. T. Edwards, FRCP

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Keywords: Magnetic resonance imaging, Image analysis, Relaxation times, Bone marrow

Abstract. A method of quantifying lumbar vertebral bone marrow using pixel by pixel T_1 mapping of spin echo magnetic resonance images is described. The accuracy and precision of the relaxation time measurements is confirmed by studies with the EEC Concerted Research Project, test object no. 5. The T_1 data from all the pixels sampled from lumbar vertebral marrow are displayed as a histogram. By "thresholding" relative to normal control data the spatial distribution of high or low T_1 pixels can be demonstrated. The approach is superior to that of the conventional region of interest method for quantifying and analysing relaxation time data, and allows tissue heterogeneity to be studied. Studies in patients with aplastic anaemia and acute leukaemia have been performed.

The large number of mobile protons present in marrow fat and haemopoietic tissue mean that bone marrow is particularly well suited to study with magnetic resonance (MR) imaging. MR allows large volumes of marrow to be examined non-invasively (Vogler & Murphy, 1988; Steiner et al, 1990), and it has been suggested that conventional spin echo MR imaging may become a clinically useful and complementary examination to the accepted "gold standard" of bone marrow biopsy in detecting bone marrow involvement in lymphoma (Linden et al, 1989).

The ability to characterize tissues on the basis of the intrinsic tissue parameters T_1 , T_2 and proton density is one of the important fundamentals of MR imaging. Studies of relaxation times measured with region of interest (ROI) cursors in thoraco-lumbar vertebral bone marrow have shown that an elevated T_1 relaxation time is associated with infiltrative marrow disorders (Nyman et al, 1987; Richards et al, 1988; Smith et al, 1989a,b). Furthermore, in disorders that affect the bone marrow focally, the variation in relaxation times across the marrow may be of diagnostic value (Smith et al, 1990). However, although an elevated T_1 is a sensitive indi-

cator of hypercellular marrow it is not specific for any particular pathology (Smith et al, 1989a).

Relaxation times are usually measured from MR images by placing operator controlled ROI cursors in areas of interest. An average T_1 , or T_2 , for the ROI is then generated from the mean signal intensities of the pixels within the ROI. However, the measurement of relaxation times using ROI cursors is subjective as it requires the operator to specify the size of the cursor and hence the number of pixels sampled, as well as the shape and position of the cursor. Jenkins et al (1989) highlighted the problems of using ROI cursors to measure relaxation times of heterogeneous tissues and have suggested that pixel by pixel analyses of MR data may be of more value. A pixel by pixel approach to the analysis of MR data has been reported in clinical studies of the intervertebral discs (Isherwood et al, 1987) and brain (Wahlund et al, 1989).

In order to eliminate the problems associated with ROI cursors, and to investigate aspects of relaxation time variation in lumbar vertebral bone marrow, we have developed pixel by pixel T_1 mapping methods. These have been used in conjunction with image analysis techniques to allow a totally objective assessment of relaxation time data obtained from lumbar vertebral bone marrow.

The pixel by pixel T_1 mapping procedure and the validation work performed with test objects, through

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which the precision and accuracy of the technique was ascertained, are described. Preliminary results obtained from normal volunteers and patients with acute leukaemia and aplastic anaemia are presented.

Materials and methods

All MR data were acquired on a 1.5 Tesla General Electric Signa system. MR images were transferred to a SUN 3/160 workstation (SUN Microsystems, USA) for computation of T_1 maps using programs written in "C". The SUN workstation is host to a GOP 302 image analysis system (Strvers AB, Sweden).

Test object studies

The accuracy and precision of relaxation time measurements, calculated by the T_1 mapping technique implemented on a SUN workstation, and by software available on the Signa system, was ascertained by serial studies of a reference phantom: the EEC Concerted Research Project test object no. 5 (TO5) (Lerski et al, 1988). This test object consists of a Perspex cylinder containing copper sulphate solution, in which 12 sealed tubes of internal diameter 20 mm can be held. The tubes contain gadolinium doped agarose gels with varying T_1 and T_2 values. The T_1 and T_2 values for the different gels had been measured in a spectrometer operating at 8 MHz and at different temperatures. Relaxation times at other frequencies were extrapolated from a mathematical model (Lerski & McRobbie, 1987).

Six studies of TO5 were performed over a 30 day period, at scan room temperatures of between 19.5 and 21.5°C. The test object was imaged in a commercially available quadrature proton head coil. A single 10 mm thick axial slice was scanned with a 128 × 256 matrix and a 24 cm field of view using conventional spin echo techniques. Each T_1 data set comprised six images with repetition times (TR) of 2400, 1600, 1000, 750, 500, 250 ms, and an echo time (TE) of 25 ms. T_1 values for TO5 were derived by both ROI and pixel by pixel methods, and compared with the reference values.

Rectangular operator controlled ROI cursors encompassing 132 pixels were placed in each tube in one of the images of the T_1 data set of TO5 and commercially available software on the Signa used to derive T_1 values. T_1 was calculated using a two parameter curve fitting algorithm assuming monoexponential relaxation processes and a 90° flip angle (Tauber et al, 1985).

On the SUN T_1 was calculated on a pixel by pixel basis according to the formula:

$$A = A_0[1 - \exp(-TR/T_1)],$$

where A is the signal intensity in the MR image obtained with repetition time (TR), and A_0 is a constant. A Newton-Raphson iterative curve fitting procedure was used and stopped for each pixel when the value of T_1 came to within 0.05% of the previous value. Generally the convergence was rapid. However, if after 10 iterations the required degree of convergence was not found then the data for that pixel were excluded from the analysis which followed. Less than 0.01% of the

bone marrow pixels failed to provide values for T_1 . The calculated T_1 values were scaled for display as 256 grey levels, where one grey level represents 9 ms.

The resolution of T_1 values obtained by T_1 mapping was illustrated by colour coding the T_1 values (mean ± 1SD) obtained from the histogram analysis of one of the studies of TO5.

Volunteer and patient studies

T_1 data sets obtained from the lumbar spine of 18 normal volunteers (age range 20–45 years; mean age 31.6 years; 11 females) were studied. A rectangular receive surface coil was placed under the lumbar vertebral bodies. The six images of the T_1 data set were obtained from a single midline sagittal slice of the lumbar vertebrae that had been prescribed from a gradient echo coronal scout scan, using the same repetition times used in the studies of TO5 (Smith et al, 1989a).

Three patients with aplastic anaemia (three male, age range 26–33 years) were studied; two had severe aplasia with bone marrow cellularities of less than 20% and both were dependent on blood and platelet transfusions, while the third patient had a moderate degree of aplasia with a marrow cellularity of 35%, and was no longer dependent on transfusions following a therapeutic response to Cyclosporin A. A 22-year-old male patient with relapsed acute lymphoblastic leukaemia whose bone marrow was completely replaced with lymphoblasts was also studied before reinduction chemotherapy.

GOP line detection algorithms were used to define the boundaries of the lumbar vertebral bodies for each subject from the proton density weighted MR image (TR/TE 2400/25 ms) of the corresponding T_1 data set. By subsequently considering only those pixels which lie completely inside those boundaries revealed by image analysis, it is certain that the amount of T_1 data obtained is maximized, but not biased, by chemical shift artefacts that might affect pixels representing the edges of the vertebral bodies. T_1 maps of lumbar vertebral marrow were displayed as grey scale images where one grey level represents 20 ms. A histogram of the distribution of the T_1 values of the lumbar vertebral marrow could then be obtained. From the histogram data the mean and median T_1 values and the total number of pixels sampled for the vertebral marrow could be measured. Contributions to the T_1 of the bone marrow come from both the fat and water elements in the pixel so that the quantity is best referred to as a bulk T_1 relaxation time. The spatial distribution of pixels "thresholded" to a specific T_1 value or range could be highlighted in colour on the T_1 map and superimposed on the original grey scale images. The area of these highlighted regions was then calculated using programs available on the GOP 302.

Results

Test object studies

The T_1 values for each of the 12 reference tubes in TO5 were averaged over the six studies and the preci-

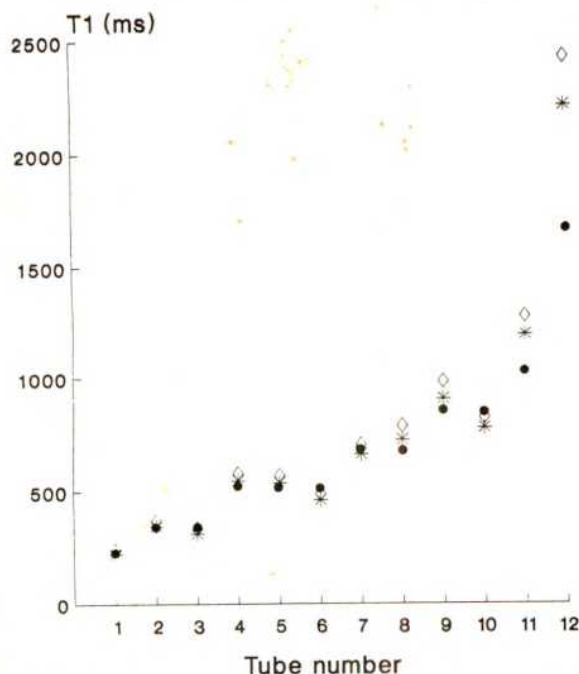


Figure 1. Accuracy of T_1 measurements obtained with the two parameter fit on the Signa system (*), and the pixel by pixel method ($\diamond$) for reference phantom (TO5). The mean of six studies performed over 30 days at temperatures of 19.5–21.5°C are shown. The reference values for the 12 tubes at 23°C are also shown (●).

sion of repeat studies expressed as percentage coefficient of variation (%CV). The reproducibility (precision) of measurements obtained from TO5 over a 30 day period was good. The %CV ranged from 0.6 to 2.2% for T_1 values obtained from the analysis of histograms, and

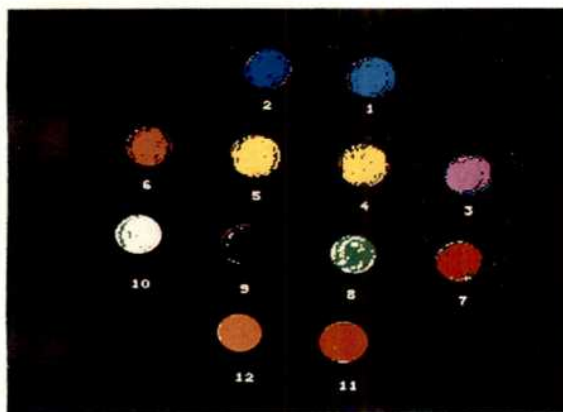


Figure 2. Colour coded T_1 map of Eurospin TO5 illustrating the T_1 resolution obtained. The scaling used in the data analysis of TO5 allowed a T_1 resolution of 9 ms, hence tubes 4 and 5 with very similar T_1 values (see Fig. 1) code in the same colour.

from 0.7 to 3.3% for values obtained from the two parameter fit available on the Signa system.

The accuracy of the T_1 measurements obtained with both the T_1 mapping technique and the Signa software was compared with reference values obtained at 23°C (Fig. 1). The agreement between T_1 values obtained from the histogram analysis and the Signa two parameter fit was generally good. The T_1 values obtained from the histogram analysis and the reference values gave a correlation coefficient of $r = 0.985$. There was a tendency for both methods to over-estimate the T_1 times of reference tubes 11 and 12 which had the highest T_1 values (see Fig. 1). The ability to discriminate between T_1 values is illustrated in Fig. 2. In this example a T_1 map obtained from a study of TO5 was colour coded to represent the mean and one SD range of T_1 obtained from histogram analyses of the reference tubes.

Volunteer and patient studies

Histograms of the T_1 data of the lumbar vertebral marrow of controls were obtained (Fig. 3). These data were recognized as exhibiting a log normal distribution and from an analysis of all the control data the T_1 values corresponding to the 5% and 95% probability limits were calculated to be 423 ms and 1596 ms respectively. Using these values as thresholds the T_1 maps of the normal volunteers were redisplayed with pixel values ≤ 423 ms or ≥ 1596 ms highlighted in colour (Fig. 4). The percentage of marrow pixels falling outside these limits was expressed as a percentage of the total pixels sampled and calculated for each individual. Mean values of 3.14% (95% confidence interval of 1.36% to 4.91%) for pixels ≤ 423 ms, and 5.84% (95% confidence interval of 3.68% to 8.00%) for pixels ≥ 1596 ms were obtained.

The 5% and 95% threshold levels calculated above from the normal volunteers were applied to the T_1 maps and histograms of the patients with aplastic and leukaemic bone marrow studied. The three patients with aplastic anaemia had histograms that were shifted to the left of normal controls, i.e. to low T_1 values and had greatly increased percentages (32–42%) of marrow pixels at or below the 5% probability limit obtained for the controls. A histogram of a patient with aplastic anaemia is shown in Fig. 5 and a corresponding spin echo MR image (TR/TE 500/25 ms) with low T_1 pixels highlighted in Fig. 6.

The histogram of T_1 data obtained from the patient with lymphoblastic leukaemia is shown in Fig. 7, with marked shift of the histogram to the right when compared with controls and a large number of high T_1 pixels is noted. An MR image with pixels equal to or above the 95% probability limit highlighted in colour is shown in Fig. 8. In this case 66% of pixels were above this threshold limit compared with an average of 5.8% in the controls studied.

Discussion

When an ROI cursor is used to define an area within tissue, the signal intensities of the pixels will be averaged

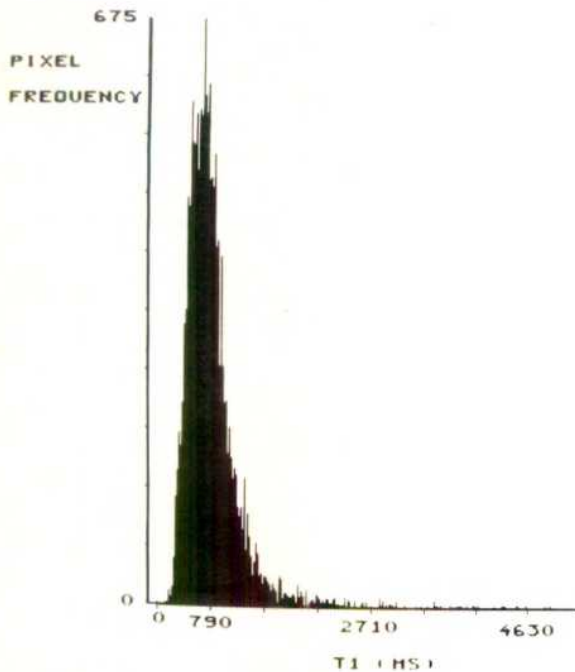


Figure 3. T_1 histogram obtained from the lumbar vertebrae of a normal volunteer (29-year-old male).

out and a mean T_1 time for the pixels within that ROI calculated. In very homogeneous normal tissues, or in disorders that affect tissue uniformly at a structural level, large ROI cursors may be adequate to provide a

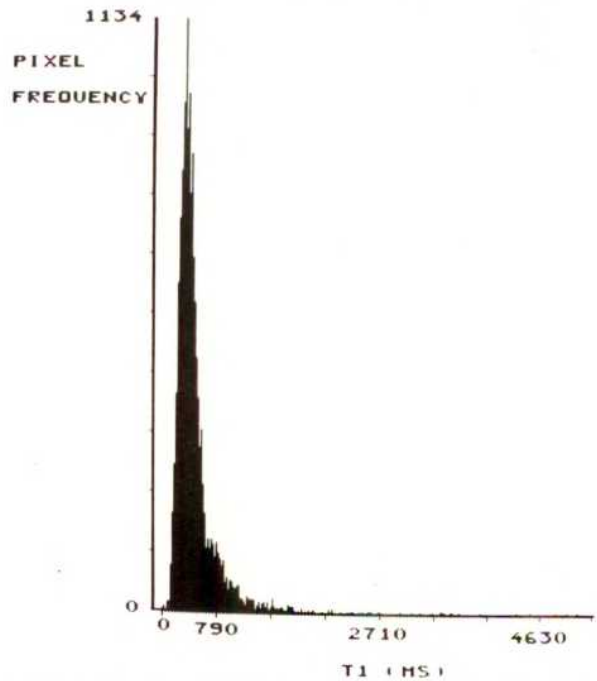


Figure 5. T_1 histogram of 26-year-old male with severe aplastic anaemia.

representative T_1 time for that tissue. This, however, will not be the case where the tissue being studied is inhomogeneous. In a recent study of lumbar vertebrae, Jenkins et al (1989) illustrated how small movements of a large

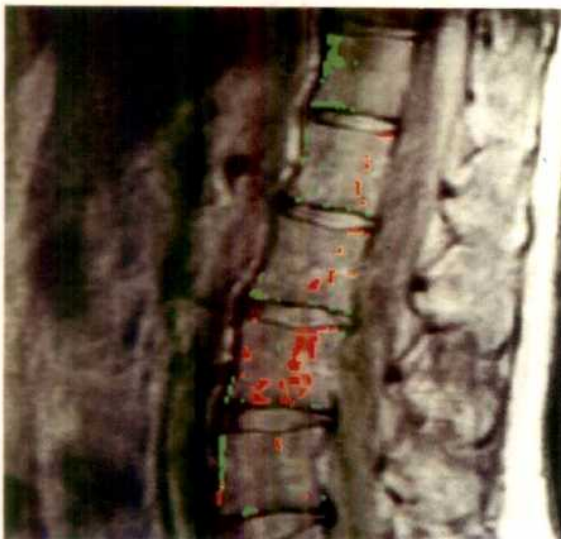


Figure 4. T_1 weighted sagittal spin echo image of the lumbar spine of normal volunteer (same patient as Fig. 3). Pixels with T_1 values ≤ 423 ms have been highlighted in red (4.9% of pixels sampled), and those ≥ 1596 ms coloured in green (3.7% of pixels sampled).



Figure 6. T_1 -weighted sagittal spin echo image of the lumbar spine of patient with aplastic anaemia (same patient as in Fig. 5). Pixels have been thresholded to the same levels as in Fig. 4 and displayed in colour. Note the large area (42%) of low T_1 (≤ 423 ms) pixels (red) when compared with controls.

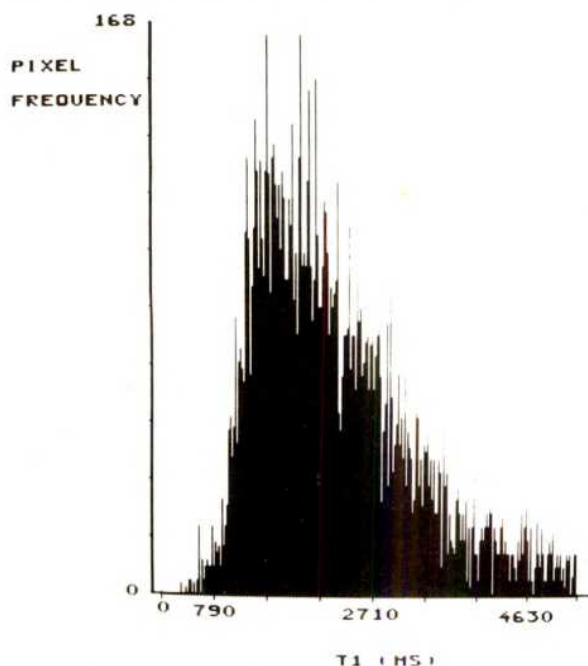


Figure 7. T_1 histogram of 22-year-old male with relapsed acute lymphoblastic leukaemia.

ROI cursor made large differences in the relaxation times obtained. Pixel by pixel relaxation time analysis allows the variation of relaxation time across the whole of the tissue of interest to be assessed. In addition, pixel

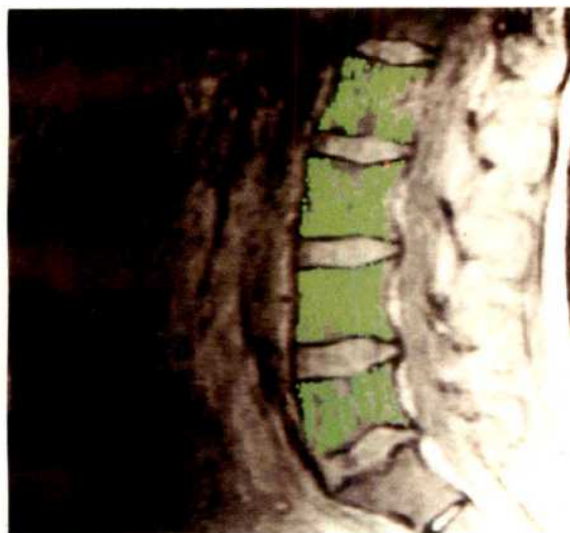


Figure 8. T_1 -weighted sagittal MR image of lumbar spine of the male patient with acute lymphoblastic leukaemia. Pixels have been thresholded to the same T_1 values as in Fig. 4. Note the very large area of high T_1 pixels (66% of pixels sampled), and the absence of low T_1 pixels.

by pixel mapping coupled with image analysis provides the means for isolating tissues of interest and for investigating spatial distribution and the patterns of T_1 abnormality.

In our study spin echo MR techniques have been used to obtain reproducible relaxation time data from the lumbar vertebral marrow. To reduce sources of error often associated with clinical relaxation time measurements multiple point calculations were used to derive T_1 and MR data were acquired from a single sagittal slice only (Smith et al, 1989a). Studies of test objects have shown that the T_1 mapping technique produces reproducible T_1 measurements which compare favourably with those reported in the literature (Breger et al, 1989). The T_1 values obtained from a pixel by pixel analysis of TO5 compared well with those obtained from ROI cursors using the facility available on the Signa. The accuracy of T_1 measurements was worse at high T_1 values for both the histogram method and the two parameter fit available on the Signa and probably reflects the range of repetition times used in this study, the maximum TR being 2400 ms.

As the boundaries of the lumbar vertebrae were delineated, using line detection algorithms with minimal operator interaction, the volume of tissue included in the T_1 analysis was delineated objectively and increased appreciably relative to conventional ROI cursors.

In bone marrow the major contributions to the MR signal are from the short T_1 fat and the long T_1 of haemopoietic tissue. The illustrative clinical cases described in this paper show how alterations in the proportions of fat and normal or abnormal haemopoietic tissue will alter the patterns of relaxation times. In aplastic anaemia there is a dramatic reduction in normal haemopoietic tissue with sometimes a virtual replacement of the marrow space with fat. This is reflected in the increased number of short T_1 pixels as seen in Fig. 6. Residual foci of active marrow may survive and when they occur regeneration may be very patchy (Gordon-Smith, 1989). Notably in the patient with aplasia responding to immunosuppressive therapy there was an increase in high T_1 pixels to 11% compared with an average of 5.8% in controls, perhaps suggesting foci of regenerative haemopoietic tissue. Investigation of the spatial distribution of these pixels by colour coding after "thresholding" potentially allows patterns of regeneration after treatment to be followed. The resolution of the spatial information obtained is dependent only on the matrix size and field of view used during data acquisition.

The histogram obtained from the lumbar vertebrae of the patient with acute leukaemia was shifted markedly to the right and showed an increase in high T_1 pixels when compared with controls. This is consistent with the bone marrow biopsy from this patient which showed that normal marrow had been totally replaced with malignant lymphoblasts. Alterations in relaxation times measured by ROI cursors have been suggested as a useful non-invasive means of assessing treatment response and cytoreduction following chemotherapy in

leukaemia and lymphoma (Moore et al, 1986; Thomsen et al, 1987; Smith et al, 1989b). A pixel by pixel analysis may allow an objective assessment of treatment response to be made and provide a non-invasive means of detecting residual marrow abnormalities as areas of high T_1 pixels.

An alternative approach to conventional ROI cursors has been described which allows detailed relaxation time analyses. T_1 mapping of relaxation time data of bone marrow may have a clinical role in the detection of bone marrow abnormalities in patients with lymphoma and other solid tumours where the presence of marrow involvement affects the treatment the patient may receive. The ability to localize abnormal marrow areas may allow accurate guided biopsy.

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Ultrasonic detection of parathyroid adenomas

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Abstract. High-resolution real time sonography was used to evaluate patients with suspected primary hyperparathyroidism. A total of 12 consecutive patients was scanned pre-operatively. The sensitivity of the procedure was 92% and the specificity 97%. In our hospital sonography is the procedure of choice for localizing enlarged parathyroid glands prior to surgical exploration.

With the increased use and availability of multichannel autoanalysers for biochemical determination, hypercalcaemia and primary hyperparathyroidism are now recognized to be much more common than previously appreciated (Heath et al, 1980). The treatment of choice in symptomatic patients, whose laboratory and clinical studies support the diagnosis of primary hyperparathyroidism, is exploration of the neck by an experienced parathyroid surgeon (Hodgson & Heath, 1981; Scholz & Purnell, 1981). Surgical exploration is also indicated in asymptomatic individuals to cure hypercalcaemia and to avoid metabolic complications such as bone demineralization, urolithiasis and nephrocalcinosis (Gaz & Wang, 1984). A wide variety of imaging techniques have been advocated for localization. These have included oesophageal cine radiography (Stevens & Jackson, 1967), computed tomography (Adams et al, 1981; Whitley et al, 1981; Stark et al, 1983; Krubsack et al, 1986), radio-isotope imaging (Gooding et al, 1986), high resolution real time ultrasound (Sample et al, 1978; Moreau et al, 1980; Barraclough et al, 1981; Jarhult et al, 1985), thermography (Samuels et al, 1972) and arteriography and selective venous sampling (Eisenberg et al, 1974; Hjern et al, 1975). Ultrasonography is considered by many to be the imaging investigation of choice (Crocker, 1986; Davidson et al, 1988) and has been reported to be a specific and sensitive test (Simeone et al, 1981; Heerden et al, 1982; Stark et al, 1985; Buchwach et al, 1987). We describe our recent experience with high resolution real time sonography in patients with primary hyperparathyroidism.

Materials and methods

During a 14 month period 12 patients with biochemical evidence of primary hyperparathyroidism and with raised serum parathyroid hormone levels were scanned before surgical exploration. The ultrasound examinations were performed using a real time ultrasound unit

(Advanced Technology Labs, Bellevue, WA) with a high resolution 7.5 MHz transducer. Scans were obtained with the patient in the supine position and the neck slightly extended. Multiple planes were scanned covering the thyroid gland and adjacent internal jugular and carotid vessels to the level of the clavicles. Views inferior and posterior to the clavicle were obtained as far as possible by angling the transducer. The average examination time was 10 min. The examination was considered positive if an oval or elongated discrete mass was found located along the posterior surface of the thyroid gland or related to the adjacent carotid artery. (Figs 1, 2, 3).

At operation, the side indicated by the scan was explored first. The tumour was sent for frozen section examination while the remaining glands were inspected.

Results

A total of 13 parathyroid adenomas (PTAs) were identified in 12 patients with primary hyperparathyroidism. Adenomas seen ranged in size from 6 to 40 mm and included one bilateral PTA, one predominantly cystic PTA (Fig. 4), one intrathyroid PTA (Fig. 5)



Figure 1. Transverse section of left neck demonstrates a 1 cm PTA (arrows) lying posterior to the thyroid (t) and common carotid artery (cc). Jugular vein (j).

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Figure 2. Longitudinal section through the right thyroid lobe showing a 2.5 cm PTA (arrows) lying posterior to the thyroid (t). Strap muscles (sm).



Figure 3. Transverse section of right neck just inferior to the lower pole of the thyroid. A 0.6 cm hypoechoic mass (crosses) consistent with a PTA lies adjacent to the common carotid artery (cc). Jugular vein (j); sterno-cleidomastoid muscle (s).



Figure 4. Longitudinal section through the right thyroid lobe (t) shows a cystic PTA (crosses), containing internal echoes and showing some posterior acoustic enhancement.

and one PTA lying between the trachea and the oesophagus. Twelve of the 13 PTAs were correctly identified by ultrasound. There was one false positive and one



Figure 5. Longitudinal section showing a PTA (crosses) lying within the thyroid capsule. Thyroid (t).

false negative examination result in one patient. At operation this patient was found to have a pedunculated thyroid adenoma at the lower pole of the right thyroid lobe which was interpreted as a PTA, and a PTA at the left lower thyroid pole which was interpreted as a thyroid adenoma. Thirty-one normal parathyroid glands were identified at operation. The sensitivity of ultrasound investigation was 92%, specificity 97% and accuracy 95%. Duration of operation ranged from 55 to 150 min (mean 79 min). All patients were rendered normocalcaemic by surgery and remained normocalcaemic for at least 3 months post-operatively.

Discussion

The results of our study compare favourably with those of other studies, which variously reported sensitivities of 63–85% (Butch et al, 1985; Jarhult et al, 1985; Gooding et al, 1986; Buchwach et al, 1987; Davidson et al, 1988; Krubsack et al, 1989; Lloyd et al, 1990) and show that these tumours can be located accurately using high resolution ultrasound. Difficulty was occasionally encountered in differentiating PTAs from thyroid adenomas protruding from the posterior surface of the thyroid, a problem which has been encountered by other authors (Sample et al, 1978; Reading et al, 1982; Jarhult et al, 1985). Identification of a PTA was facilitated if a plane of cleavage or an echogenic line could be seen between the mass and the thyroid.

The choice of pre-operative imaging technique in primary hyperparathyroidism is ultimately dependent on the expertise and equipment available. Parathyroid ultrasound in particular is heavily dependent on the experience of the operator (Lloyd et al, 1990). Oesophageal cine radiography and thermography are of historical interest only. Selective venous sampling and selective arteriography are technically difficult, expensive, time consuming and potentially hazardous, but have a place in localizing PTAs in cases of failed neck exploration. Radio-isotope imaging using thallium-technetium computer subtraction scanning may identify 70–90% of parathyroid tumours (Fine, 1987; Carmalt

et al, 1988). False negative results may be obtained with isotope scanning if the glands are small, and false positive results can arise in patients with thyroid nodules (Fine, 1987). The procedure is minimally invasive but does expose the patient to radiation (Duh et al, 1987). Initial attempts using computed tomography (CT) for parathyroid tumour localization were not particularly sensitive, detecting 50 to 60% of tumours (Adams et al, 1981; Whitley et al, 1981). A major problem is streak artefact caused by shoulder positioning but this can be overcome by employing a shoulder positioning device (Stark et al, 1983). More recent reports have shown that 70 to 80% of parathyroid tumours can be detected using CT (Krubsack et al, 1989). CT has the advantage of being able to locate ectopic glands in the mediastinum where ultrasonic visualization is poor (Duh et al, 1987).

Several recent reports have advocated chemical ablation of PTAs under radiological guidance particularly for patients who are unfit for surgery, those who refuse surgery (Karstrup et al, 1987) and for those who have previously undergone unsuccessful surgery. Methods proposed include injection of ethanol under ultrasound control (Solbiati et al, 1985; Karstrup et al, 1990) and angiographic ablation by infusion of ionic contrast agents (Miller et al, 1987). The emergence of these techniques illustrates the importance of pre-therapy imaging and in particular the role of ultrasound as a method of localization.

An experienced parathyroid surgeon can successfully cure 90–95% of patients with hyperparathyroidism without the pre-operative use of a localization procedure (Satava et al, 1975; Rossoff, 1985). Because of this some clinicians consider pre-operative localization unnecessary. However, using pre-operative localization a cure rate of 98.8% has been achieved (Lloyd et al, 1990) suggesting that even with an experienced parathyroid surgeon the results may be improved with pre-operative imaging. Ultrasound has undoubtedly modified the pre-operative management and operative strategy in patients with primary hyperparathyroidism in our hospital. By first exploring the side of the lesion indicated by the scan we have achieved shorter operating times than those commonly reported (Brewer et al, 1983). Shorter operating times should enable the surgical team to make more efficient use of the operating room and by minimizing the extent of tissue dissection should reduce the risk of operative complications.

In conclusion we consider ultrasound to be the imaging technique of choice for detecting PTAs because of its high accuracy, ease of application, lack of radiation and relatively low cost. Pre-operative localization of PTAs in our practice facilitates surgical exploration for primary hyperparathyroidism.

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Magnetic resonance imaging in the staging of renal cell carcinoma

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Abstract. A prospective study has been carried out to examine the role of magnetic resonance imaging (MRI) in the investigation of renal cell carcinoma in 24 patients. In all cases the inferior vena cava (IVC) was well demonstrated with MRI. In 14 out of 15 patients where surgical correlation was available, the MRI and operative staging were in agreement. Magnetic resonance imaging and computed tomographic (CT) staging were in agreement in 16 out of the 17 patients where both were performed. In one case, CT suggested hepatic invasion but this was found not to be present on MRI and at operation. Magnetic resonance imaging also provided substantial additional information in three patients, including two cases where MRI demonstrated a patent IVC that appeared occluded on CT (one of which also had vertebral metastases seen on MRI but missed on CT) and one case where CT failed to demonstrate minimal involvement of the IVC. Magnetic resonance imaging is an accurate means of staging renal cell carcinoma with clear advantages over CT. In no case in this series was inferior vena cavography found to be necessary.

In the vast majority of patients with suspected renal cell carcinoma, intravenous urography (IVU) and ultrasound will produce the diagnosis (Demas et al, 1988), occasionally with the addition of percutaneous biopsy. Further investigations will generally be directed towards staging the tumour.

Involvement of the renal vein and inferior vena cava (IVC) will affect the surgical technique used (McDonald, 1982; Woodhouse et al, 1985; Pritchett et al, 1986) and the presence of invasion of regional lymph nodes or viscera and distant metastases has considerable prognostic significance (Skinner et al, 1972; Boxer et al, 1979; Lieber et al, 1981).

Both ultrasound and computed tomography (CT) (especially dynamic CT) can be used to evaluate the IVC, regional lymph nodes and local invasion of the tumour. Although an accuracy of up to 91% for CT has been reported (Johnson et al, 1987), an accuracy of 72-78% may be more realistic (Frohmuller et al, 1987; Didier et al, 1987; London et al, 1989; Miles et al, 1990). Problems with CT include inadequate or mistimed injection of intravenous contrast medium and limitations of the transverse plane of the section may result in difficulty in evaluating the interface between the tumour and adjacent viscera (Demas et al, 1988).

The purpose of this study was to determine the accuracy of magnetic resonance imaging (MRI) staging of renal cell carcinomas, in particular with reference to IVC involvement and to see if inferior vena cavography can be regarded as obsolete in this situation.

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Methods

Magnetic resonance imaging was performed on 24 patients with renal cell carcinoma. A T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) in transverse and coronal planes and a STIR (short tau inversion-recovery) sequence (TR 1900 ms, TE 30 ms, TI 100 ms) in the coronal plane were performed using a Picker Vista 2055 HP 0.5 T scanner. Further sequences in additional planes were performed depending on the appearances on the standard views. The tumours were staged using the conventional classification described by Robson et al (1969) (Table I). The results were compared with operative findings in 15 cases. In 17 cases comparison with CT was available but only 11 of these were operated on. The CT scans were performed on a Siemens Somatom DRH or a GE 9000 in one of two referring hospitals using 10 mm consecutive cuts through the kidney immediately following an intravenous injection of 50 ml of Iopamidol 370 mg/ml. In three patients who did not undergo surgery, only MRI and ultrasound were performed.

Table I. Staging of renal cell carcinoma (Robson et al 1969)

Stage	
I	Limited by the renal capsule
II	Perirenal involvement including the adrenal but limited by Gerota's fascia
IIIa	Involvement of renal vein or IVC
IIIb	Involvement of regional lymph nodes
IIIc	Vascular and lymphatic involvement
IV	Invasion of adjacent viscera or distant metastases



Figure 1. Coronal T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing normal renal architecture on the left; medium-signal-intensity cortex, low-signal-intensity pyramids. This is replaced in the mid and upper part of the right kidney by medium-signal-intensity tumour (vertical arrow). Note similar signal intensity lymph node immediately adjacent to the right lateral border of the first lumbar vertebra (horizontal arrow).

Results

In all 24 cases the IVC was well demonstrated on MRI. The renal cell carcinomas produced a signal intensity similar to renal tissue on all sequences and therefore were seen as masses of medium signal intensity (slightly higher than the signal from skeletal muscle) on T_1 -weighted sequences and high signal on STIR sequences (Figs 1 and 2). T_1 -weighted sequences demonstrated normal renal architecture well and this was lost in areas occupied by tumour. A common finding was a leash of low-signal-intensity vessels lying just outside the margins of the tumour and presumably representing collateral blood supply or parasitic neovascularization

Table II. MRI staging of 24 renal cell carcinomas

Stage	Number
I	8
II	2
IIIa	2
IIIc	1
IV	11*
Total	24

*Includes four with renal vein involvement, two of which showed tumour extension into the IVC.

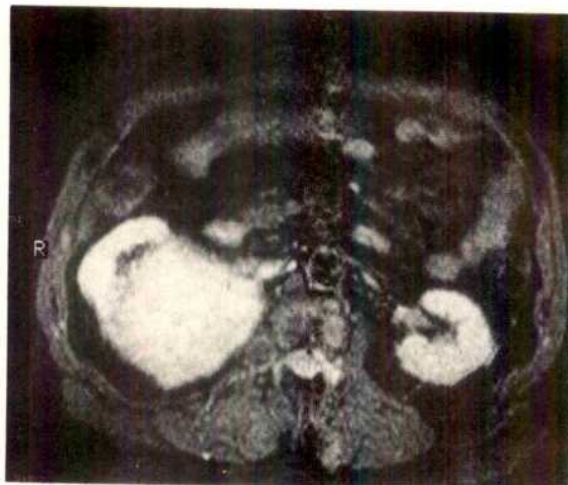


Figure 2. Transverse STIR sequence (TR 1900 ms, TE 30 ms, TI 100 ms) showing high signal intensity from the normal kidney and the large renal carcinoma, seen protruding from the posteromedial aspect of the right kidney.

of the carcinoma (Demas et al, 1988; Choyke & Pollack, 1988) (Fig. 3).

The MRI staging of the tumours is shown in Table II. They included seven patients with renal vein involvement, five of whom showed extension into the IVC. Three patients with locally operable disease (all Stage I on MRI) did not undergo surgery: in two cases because of ultimately fatal medical conditions (cerebrovascular accident in one patient, bronchopneumonia on a background of chronic obstructive airways disease in the

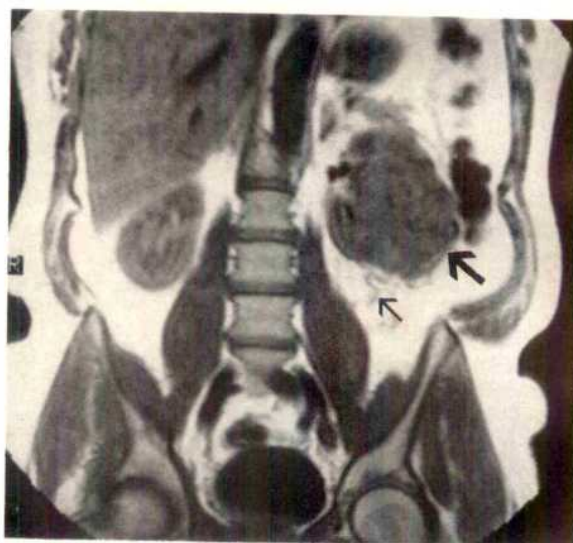


Figure 3. Coronal T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing a leash of new vessels (small arrow) related to the inferior aspect of the left renal cell carcinoma (large arrow).

Table III. Operative and MRI staging

	Operative	MRI
Renal vein involved	6	5
IVC involved	5	5
Overall stage		
I	6	5
II	1	2
IIIa	2	2
IIIc	1	1
IV	5	5
Total	15	15

other) and in one case because the tumour was in a solitary kidney. Surgery was not performed in six patients with Stage IV disease, in three cases because of distant metastases (two skeletal and one hepatic) and in three cases because of very extensive local tumour.

Operative correlation therefore was available in 15 patients. Comparison with CT was available in 17 patients. In three patients only ultrasound was available to correlate the MRI demonstration of an uninvolved IVC.

In the 15 patients where operative findings were available, the MRI stage agreed with the pathological stage in 14 cases. In one case a Stage I tumour was classified as Stage II on MRI and CT. In all these cases MRI defined accurately IVC involvement and the presence or absence of invasion of regional lymph nodes and adjacent viscera. In one case (overall Stage IV) the MRI was not of sufficiently good quality to be confident of the state of the renal vein, and at operation it was shown to be involved proximally by tumour.

The staging of these patients is shown in Table III. The overall staging accuracy of MRI compared with operation was 93%, its specificity and sensitivity for IVC involvement being 100%.

In the 17 patients where CT correlation was available, there was agreement with the overall MRI stage in 16 cases. In one case CT suggested hepatic invasion by the tumour, shown not to be present on MRI and at operation.

Both MRI and CT suggested a Stage I tumour was Stage II. In two further cases, CT suggested extensive IVC invasion by tumour but MRI demonstrated a compressed but patent IVC (Fig. 4). In one of these patients MRI elegantly demonstrated vertebral metastases not seen on CT (Fig. 5) and in another case MRI defined the upper limit of IVC involvement, which ultrasound and CT had been unable to do (Fig. 6). In one further case CT failed to demonstrate a nodule of tumour in the IVC, shown on MRI and at operation (Fig. 7). This, however, did not change the stage of these tumours.

In one patient both MRI and CT demonstrated an irregular tumour continuous with the peritoneum in the presence of ascites. The assumption was made that this was a Stage IV tumour rather unusually directly invading the peritoneum. Unfortunately the patient died

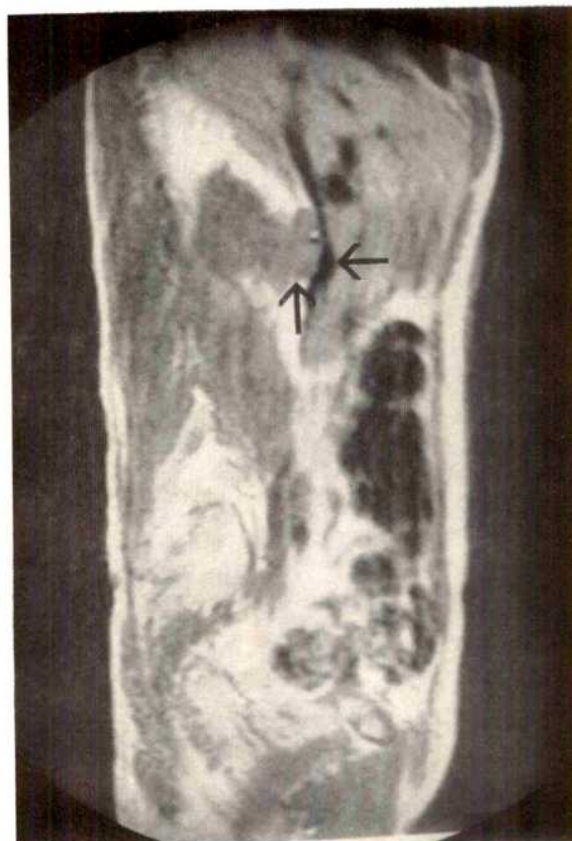


Figure 4. Sagittal T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing extension of tumour (vertical arrow) behind a patent IVC (horizontal arrow), producing forward deviation of the vessel.

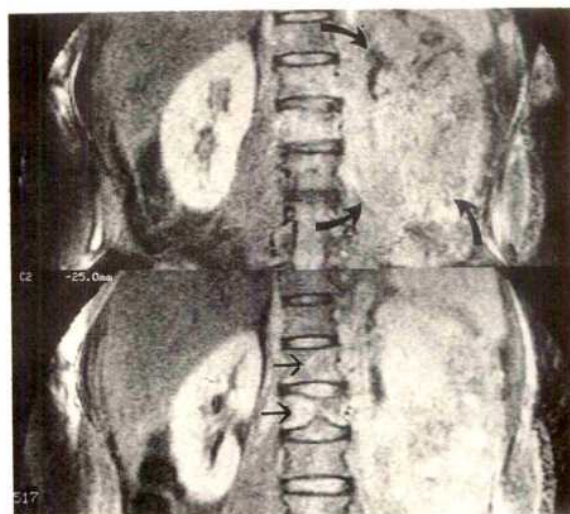


Figure 5. Coronal STIR sequence (TR 1900 ms, TE 30 ms, TI 100 ms) showing a large left renal cell carcinoma of mixed but predominantly high signal (curved arrows) and high-signal vertebral metastases (horizontal straight arrows).



Figure 6. Coronal T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing right renal cell carcinoma with extension along the right renal vein and into the IVC up to the level of the diaphragm.

without operation and no post-mortem examination was performed. Renal adenocarcinoma cells were, however, demonstrated in the ascites.

There was agreement between CT and operative staging in nine out of 11 patients where both were performed, giving a CT accuracy of 82% (Table IV). The two cases of disagreement are described above.

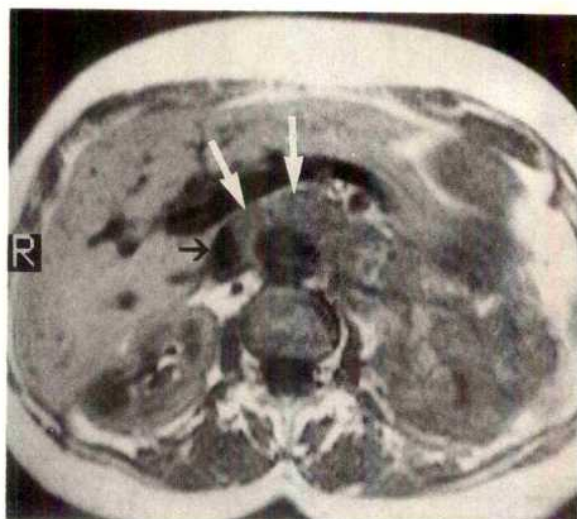
In three patients who did not undergo surgery (two Stage IV, one Stage I) only ultrasound and MRI were performed; both demonstrated an absence of IVC involvement.

Discussion

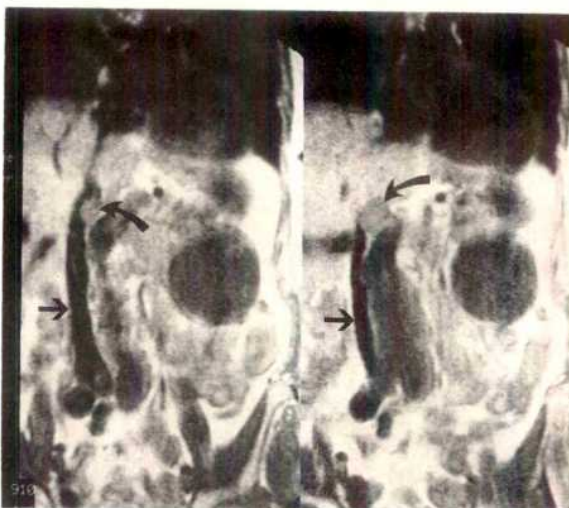
A variety of methods is available for staging renal cell carcinoma. Excretion urography and angiography are at best 59% and 57% accurate, respectively (Frohmüller et al, 1987). Ultrasound is almost invariably performed as part of the diagnostic process for renal cell carcinomas.

Table IV. Operative and CT staging

	Operative	CT
Stage		
I	4	3
II	1	2
IIIa	2	2
IIIc	1	0
IV	3	4
Total	11	11



(a)



(b)

Figure 7. (a) Transverse and (b) coronal T_1 -weighted spin-echo sequences (TR 600 ms, TE 26 ms) showing tumour extending along an expanded left renal vein [white arrows, Fig. 7(a)]. Tumour is seen to just protrude into the patent IVC [black horizontal arrows, (a) and (b)]. In the coronal plane the nodule of tumour entering the IVC from the left renal vein is well shown [curved arrows, Fig. 7(b)].

Its accuracy for staging is up to about 78% (Frohmüller et al, 1987), with some studies suggesting a lower figure of around 50% (London et al, 1989). Excess bowel gas and adverse patient build may prevent an adequate examination. Clearly the performance of an ultrasound examination depends on the operator's skill but all means of staging are to some extent subjective.

Although Johnson et al (1987) reported an accuracy of 91% for CT staging (using a dynamic contrast technique) a number of comparative studies have suggested much lower values. Frohmüller et al (1987) reported a

staging accuracy of 78% for ultrasound compared with 72% for CT (although the CT technique used is not described). More recently, London et al (1989) reported a 50% accuracy for conventionally enhanced CT and 72% accuracy for dynamic CT. The lower figure for conventionally enhanced CT may be partly due to their technique of performing the post-contrast scan 5 minutes after the intravenous injection. The same group of workers suggest a single-location dynamic scan in addition to an incremental scan during infusion of intravenous contrast medium may increase CT accuracy above 72%, especially for the vascular stage (Miles et al, 1990).

In addition to the general problems of CT compared with ultrasound or MRI (the use of intravenous iodine-containing contrast media and ionizing radiation), diagnostic errors in CT staging may arise because of the limitations of scanning only in the transverse plane especially when dealing with polar tumours (Demas et al, 1988). Using strict CT criteria—change in organ size or density—adjacent organ invasion is only identified in 60% of cases; diagnosing invasion on the basis of a loss of fat line alone results in a rate of false positives of around 15% (Johnson et al, 1987; Demas et al, 1988).

Although inferior vena cavography can detect IVC and renal vein involvement with an accuracy of 93% and 88%, respectively (Horan et al 1989), it offers no information about local invasion and only detects lymph nodes sufficiently enlarged to impinge on the IVC. Horan et al (1989) compared MRI accuracy for vascular staging with inferior vena cavography and found it was not significantly different (MRI accuracy for IVC and renal vein involvement being 93% and 86%, respectively).

Our study examined the role of MRI in the investigation of renal cell carcinomas. The tumours were found to have a medium signal on T_1 -weighted sequences and high signal intensity on the STIR sequence. This was very close to the signal from normal renal tissue. The similarity between signal from normal kidney and tumour on all sequences including proton density and T_2 -weighted sequences has been noted before (Quint et al, 1988). Tumours, therefore, are not generally visible on MRI until they are large enough to distort renal architecture (well seen on the T_1 -weighted sequence in high-quality scans; Fig. 1) or the renal outline (Quint et al, 1988; Choyke, 1988).

A number of studies have described the use of MRI in studying renal disease. It was quickly realized that MRI could identify focal renal masses and distinguish solid from cystic lesions (Choyke et al, 1984). Although initially it was thought that histologically specific signals might be obtainable from renal tumours (Hricak et al, 1983), this promise has not yet been fulfilled and differentiation between benign and malignant renal tumours cannot be made on the basis of signal intensity (Hricak et al, 1988).

The accuracy of MRI staging of renal cell carcinoma has been reported at 82–96% (Hricak et al, 1985, 1988). The overall accuracy in the 15 patients in this current

study was 93%. The single error of staging was mistaking a Stage I tumour for Stage II and was also made on CT. Others have reported this difficulty with both techniques (Fein et al, 1987; Johnson et al, 1987) and it is likely that at the current stage of development neither CT nor MRI can reliably distinguish between Stage I and Stage II. It is, however, not a significant problem since the prognosis and treatment of both categories of tumour are virtually identical unless a partial nephrectomy is being planned (Robson et al 1969; Boxer et al, 1979; Guiliani et al, 1990).

In all patients studied, the IVC was well seen. In five patients undergoing surgery, IVC involvement was present and accurately defined. In one further case with proximal renal vein involvement the MRI was not of sufficiently good quality to stage the renal vein. Because of the signal void in flowing blood, patent vessels are easily seen in good-quality scans and vascular invasion by tumour is elegantly demonstrated by MRI (Karstaedt et al, 1986; Fein et al, 1987; Pritchett et al, 1987). The MRI sensitivity for distal renal vein and IVC involvement is around 100%, sensitivity and specificity for proximal renal vein involvement being 86 and 96%, respectively (Hricak et al, 1988). In this group of patients the operative approach depends on adequate demonstration of the intravenous extension.

The prognosis for renal vein extension alone is probably similar to that for Stage I disease (Skinner et al, 1972); the prognosis for patients with IVC involvement is still debated. Some studies suggest it approaches that of Stage I disease (Skinner et al, 1972; Boxer et al, 1979; Cherrie et al, 1982; Pritchett et al, 1986). Other studies are more pessimistic (Robson et al, 1969; Kearney et al, 1981). The most recent and one of the largest studies (Guiliani et al, 1990) shows a poor prognosis with IVC involvement, similar to that for patients with distant metastases.

Neither ultrasound nor CT can distinguish tumour or thrombus extension into the IVC from invasion of the vessel wall (Didier et al, 1987) and there is no evidence to suggest MRI can either.

Although the operative approach may be unaffected by the presence of involved lymph nodes, this has a significant effect on prognosis (Skinner et al, 1972; Guiliani et al, 1990). Two patients in this study had extensive para-aortic lymphadenopathy and did not undergo operation. In both, the CT scan suggested IVC occlusion but MRI demonstrated a patent, albeit compressed and deviated, IVC.

Of the 15 patients undergoing surgery in this series only one had regional lymph node involvement by tumour (Fig 8.) and this was correctly predicted by both MRI and CT. Only limited comments can be made on the basis of this experience but it is probable that MRI will be at least as accurate as CT in detecting involved lymph nodes. Hricak et al (1988) reported an accuracy of 99% in predicting lymph node involvement pre-operatively with MRI. They considered any lymph node in the perivascular or perihilar areas with a diameter above 10 mm (plane not specified) to be involved,

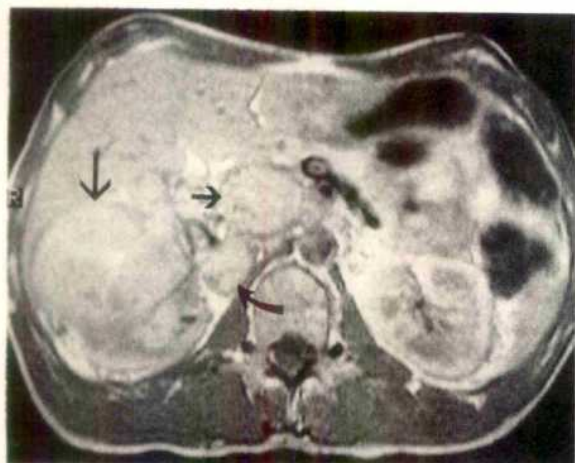


Figure 8. Transverse T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing an enlarged lymph node (curved arrow) lying medial to the right kidney (containing a large renal cell carcinoma anterolaterally, vertical arrow) and posterior to an expanded IVC occluded with tumour thrombus (horizontal arrow).

commenting that previously they had encountered lymph nodes between 10 and 15 mm diameter that were involved with tumour. Collateral vessels with their signal void on MRI are unlikely to be confused with lymph nodes (Fein et al, 1987). However, MRI and CT are both currently unable to distinguish reactive lymph

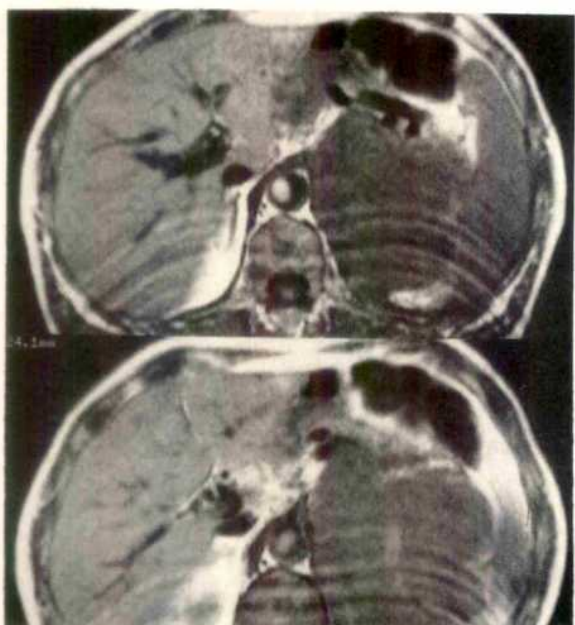


Figure 9. Transverse T_1 -weighted spin-echo sequence (TR 600 ms, TE 26 ms) showing a large left renal cell carcinoma invading the left diaphragmatic crus.

node enlargement from those involved with tumour (Choyke & Pollack, 1988; Hricak et al, 1988).

In two patients who did not undergo surgery, bone metastases were identified on MRI scans. Although skeletal secondaries can occur outside the area of the scan, the routine inclusion of much of the marrow-containing skeleton in MRI scans of the kidneys and IVC increase the chance of such metastases being identified coincidentally.

Magnetic resonance imaging correctly staged five patients undergoing surgery as Stage IV (Fig. 9). The ability of MRI to produce images in multiple planes as well as the use of different sequences gives it an advantage over CT in identifying local visceral invasion (Hricak et al, 1988; Demas et al, 1988). This is almost certainly present if there is a change of signal intensity or morphology in the adjacent organ and invasion is likely if there is loss of the normal sharp change in signal intensity at the interface between tumour and adjacent viscera (Hricak et al, 1985). Magnetic resonance imaging has been shown to have an accuracy of up to 97–100% for demonstrating direct invasion of a wide range of structures including liver, spleen, psoas and back muscles, mesentery and bowel, although in a study with a relatively small number of Stage IV tumours (Hricak et al, 1988). False positives and false negatives were also encountered in that study, particularly with respect to missing invasion of mesentery and bowel.

Conclusion

Magnetic resonance imaging is an accurate means of staging renal cell carcinoma, particularly with respect to IVC involvement. Ideally, pre-operatively, a patient with renal cell carcinoma requires an intravenous urogram, renal ultrasound, chest radiography, an MRI scan and no other routine imaging. Where MRI is available neither CT nor inferior venacavography are required.

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Non-specific aorto-arteritis (Takayasu's disease) in children

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Abstract. Digital subtraction panaorto-arteriography was performed in 32 consecutive children (21 females, mean age 10.8 years) with non-specific aorto-arteritis to assess digital subtraction angiography (DSA) in imaging these children and to study the patterns of involvement in the Indian sub-continent. Diagnostic quality DSA images were obtained in 21 out of 27 intravenous and nine out of 11 intra-arterial studies. Obstructive lesions were present in all the patients and commonly involved the abdominal aorta (24 patients) and renal arteries (20 patients). Aneurysms were seen in five patients and predominantly involved the descending thoracic aorta. Pulmonary artery involvement was uncommon (five out of 20 patients) and clinically silent. Based on clinical and angiographic features, percutaneous transluminal angioplasty was performed for the management of uncontrolled hypertension in eight patients (10 lesions). Initial success was obtained in eight procedures (80%). Re-stenosis occurred after 5.5 months in one patient, but was successfully re-dilated. The follow-up period ranged between 5 and 16 months (mean 9 months). Long-term efficacy of transluminal angioplasty in the management of these children is awaited.

Non-specific aorto-arteritis (Takayasu's disease) is a chronic and progressive disease of unknown aetiology commonly involving the aorta, its major branches and the pulmonary arteries (Hachiya, 1970; Das et al, 1982; Yamato et al, 1986), resulting in stenosing, dilative or aneurysmal lesions and these have well known racial and geographic predilections (Domingo et al, 1967; Deutsch et al, 1974; Liu, 1985; Sharma et al, 1990). It is more common in the Orient but has a worldwide distribution. It predominantly occurs in young women and involvement of children has been only occasionally reported (Golding et al, 1977; Cremin et al, 1978; Wigginkhuizen & Cremin 1978; Shrivastava et al, 1981; Gupta et al, 1981; Gronemeyer & DeMello, 1982; Haas & Stiehm, 1986).

Total aortography is mandatory for diagnosis and the arteriographic features in adult patients are well documented (Gotsman et al, 1967; Lande & Rossi, 1975; Yamato et al, 1986). Angiographic evaluation in non-specific aorto-arteritis presents certain specific problems. It is often difficult to select the site for arterial catheterization owing to frequent occurrence of obstructive disease in the abdominal aorta and the subclavian arteries. Catheter manipulation in the presence of severe underlying arterial disease presents an additional hazard. Intravenous digital subtraction angiography (IV-DSA) is, therefore, ideally suited for imaging these patients and advantages and limitations of IV-DSA in imaging adult patients have been recently reported

(Matsunaga et al, 1987; Yamamoto et al, 1987; Sharma et al, 1989). The use of IV-DSA in imaging young children and the comprehensive angiographic profile in these children have not been reported. The response of suitable arterial obstructions to percutaneous transluminal angioplasty in children has also not been described (Saddekni et al, 1980; Hodgkins & Dutton, 1982; Hiramatsu et al, 1983; Cook et al, 1986; Dong et al, 1987; Khalilullah et al, 1988; Staller & Maleki, 1989; Park et al, 1989).

Patients and methods

During last 36 months, we performed panaorto-arteriography in 32 patients with non-specific aorto-arteritis aged 16 years and under using DSA on a commercially available Angiotron CMP (Siemens) unit. The diagnosis of non-specific aorto-arteritis in each patient was based on the guidelines established by the Aortitis Syndrome Research Committee of Japan (Inada et al, 1976). Middle aortic syndrome, William's syndrome, neuro-fibromatosis and congenital vascular malformation were excluded, as were patients with single-vessel involvement with a normal aorta.

All the patients were considered for an initial IV-DSA and the intra-arterial (IA) route was chosen if IV-DSA was diagnostically inadequate or contra-indicated. The criteria for selection for IV-DSA included absence of any clinical evidence of congestive cardiac failure, a normal-sized heart shadow on a conventional chest radiograph, and a patient who was old enough to respond to breath-holding instructions. We followed a previously reported examination technique and protocol for DSA evaluation of these patients (Sharma et al, 1989). Based on the sites of involvement, the patients

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Table I. Angiographic features in 32 children

Type	Angiographic features	Number of patients	%
1	Involvement of branches of aortic arch only	1	3.1
2	Involvement of thoracic aorta and its branches only	4	12.5
3	Involvement of abdominal aorta and its branches only	8	25.0
4	Extensive involvement of whole length of aorta and/or its branches	19	59.4

were divided into four types (Yamato et al, 1986) (Table I).

Patients with 70% or more luminal diameter narrowing in the renal artery or the abdominal aorta underwent an intra-arterial study. Based on clinical and angiographic findings, the patients with arterial stenosis and trans-stenotic pressure gradient of 20 mmHg or more in the clinical setting of systemic hypertension, uncontrolled with drugs or needing multiple drugs for adequate control, were chosen for PTA. The erythrocyte sedimentation rate (ESR) was measured in all these patients; a raised ESR was considered as suggestive of "active" disease, and PTA was performed when the disease was considered "stable" after estimating the ESR. All the patients undergoing PTA were started on oral aspirin (175 mg on alternate days) and dipyridamole (25 mg three times a day) 3 days before PTA and continued for 6 months after the procedure.

Transluminal angioplasty was performed by the transfemoral route by a standard exchange technique involving the replacement of a diagnostic A-2 femoral-visceral catheter (Cordis Corp., USA) by a commercially available appropriate-sized balloon catheter (Medi-Tech Inc., USA) over an exchange guidewire (USCI International, USA). Care was taken not to use oversized balloon catheters during this study. Inflation was performed by hand using a 10 ml syringe filled with

Table II. Major clinical features in 32 children

	Number of patients	%
Hypertension	24	75.0
Absent or diminished peripheral pulses	23	71.8
Bruit	23	71.8
Dyspnoea, palpitations	20	62.5
Congestive cardiac failure	12	37.5
Constitutional symptoms	6	18.7
Claudication of lower extremities	4	12.5

Table III. Modes of angiographic evaluation

Type of angiogram	Number of patients studied	Diagnostic angiogram (%)
Intravenous DSA	27	21 (77.8)
Intra-arterial DSA	11	9 (81.8)
Conventional film-screen angiogram	2	2 (100)

DSA = digital subtraction angiogram.

30% urografin. The balloon was inflated for 30 seconds after the disappearance of the "waist" followed by a more prolonged dilatation for up to 60 seconds. The patients received 100 i.u. heparin/kg body weight during the procedure and were subsequently heparinized for 24 hours. Immediate post-procedure pressure measurement and diagnostic angiograms were obtained in all the patients in order to assess the adequacy of angioplasty. The systemic blood pressure was monitored in the next 24 hours and anti-hypertensive drugs were withheld during this period.

Transluminal angioplasty was considered as "technically successful" if the arterial lumen became normal or there was less than 30% residual stenosis, and if the trans-stenotic pressure gradient had disappeared or was

Table IV. Sites of arterial involvement ($n = 32$)

Vessels involved	Number of patients	%
Aortic arch	3	9.4
Thoracic aorta	13	40.6
Abdominal aorta	24	75.0
Renal arteries	20	62.5
Renal arteries, unilateral	10	31.25
Renal arteries, bilateral	10	31.25
Subclavian artery	13	40.6
Subclavian artery, left	10	31.25
Subclavian artery, right	1	3.1
Subclavian artery, both	2	6.2
Left carotid artery	5	15.6
Superior mesenteric artery	6	18.7
Innominate artery	2	6.2
Femoral artery	4	12.4
Aneurysm formation	5*	15.6
Descending thoracic aorta	4	—
Abdominal aorta	1	—
Left common iliac artery	1	—
Right renal artery	1	—
Pulmonary artery ($n = 20$)	5	25.0
Obstruction of lobar branch	3	—
Peripheral pruning of both pulmonary arteries	2	—

*Two patients had multiple aneurysms.

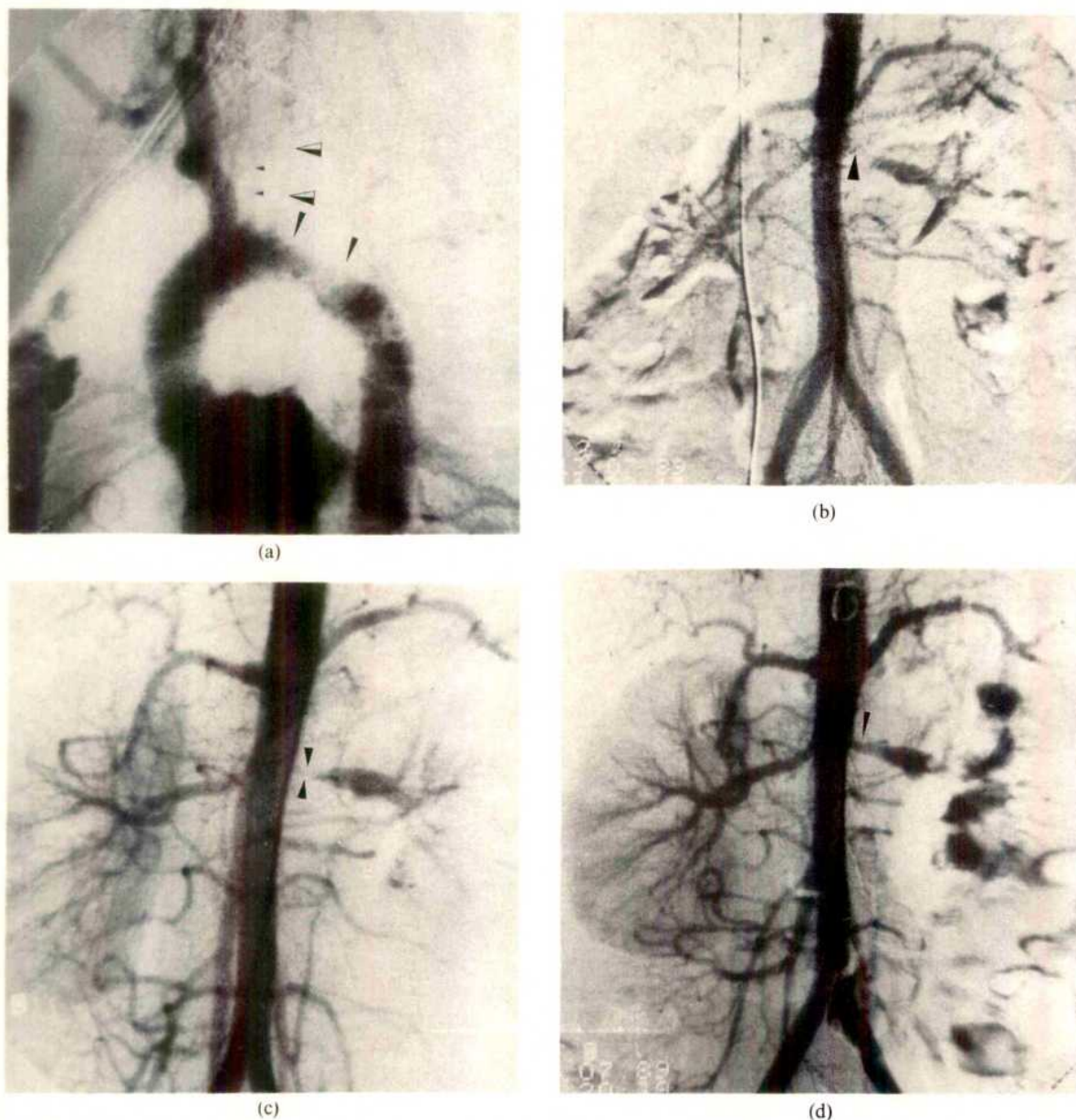


Figure 1. (a) IV-DSA of the aortic arch in the left anterior oblique (LAO) view showing mild narrowing of the aortic arch (large arrowheads) and long segment diffuse narrowings involving the left carotid (small arrowheads) and left subclavian (open arrowheads) arteries. (b) IV-DSA for the abdominal aorta in the antero-posterior (AP) view showing a tight proximal narrowing of the left renal artery (arrowhead) with post-stenotic dilatation. (c) IA-DSA for the abdominal aorta in the same patient prior to transluminal angioplasty for the left renal artery stenosis (arrowheads). (d) IA-DSA for the abdominal aorta after angioplasty showing no significant residual stenosis (arrowhead). The trans-stenotic pressure gradient before angioplasty was 100 mmHg and after angioplasty was 15 mmHg.

less than 20 mmHg. The result of angioplasty was interpreted as a "cure" if the blood pressure remained normal after the procedure without any anti-hypertensive drugs, "improved" if there was 15% reduction in pressure or if the diastolic pressure was 90 mmHg or less

with the patient receiving less anti-hypertensive medication than previously, and "failed" if PTA resulted in no change in the pre-procedure blood pressure and drug requirement (Klinge et al, 1989; Tach & Sos, 1989). Follow-up examinations were done at 24 hours, 1 week,

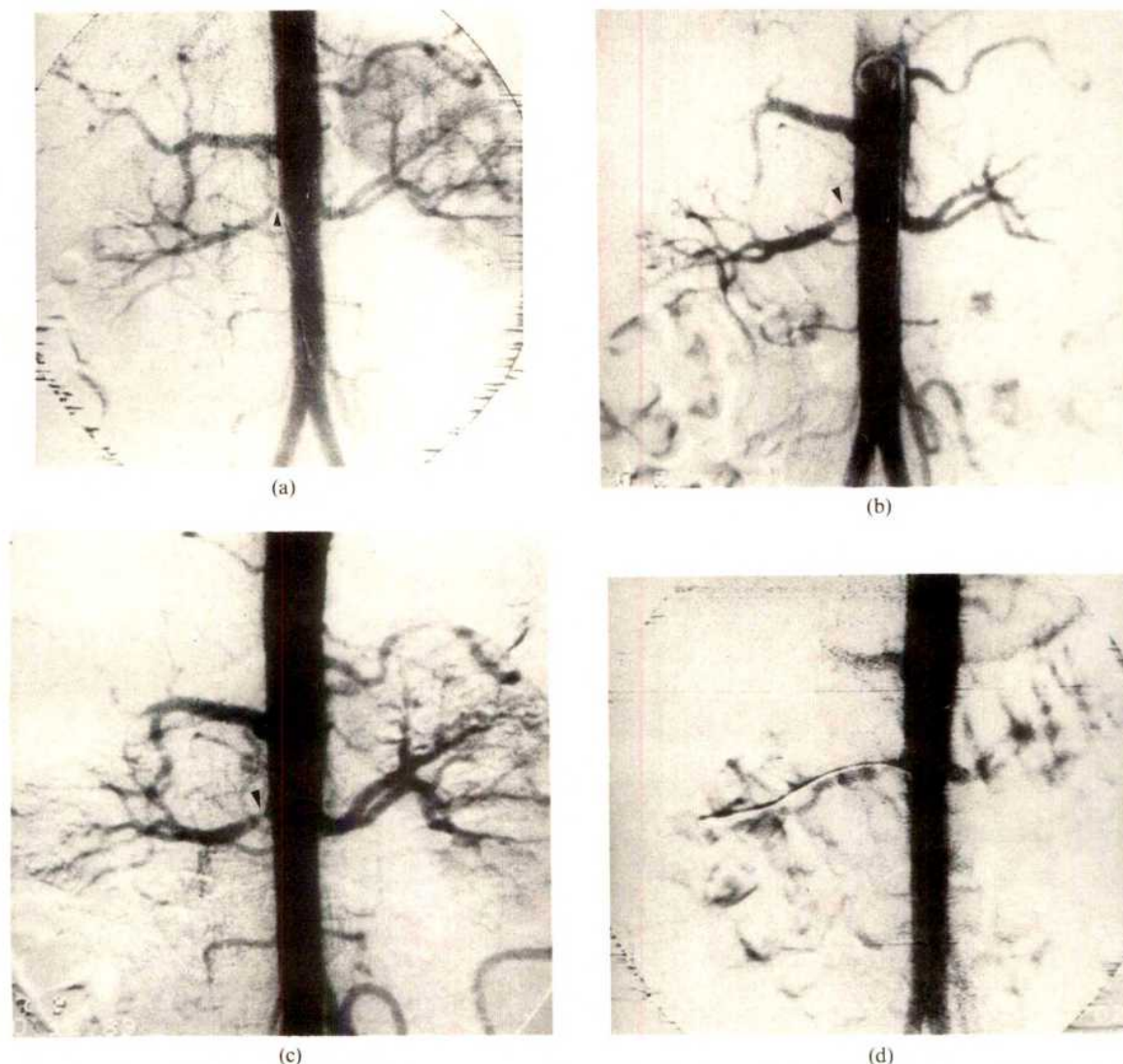


Figure 2. (a) IV-DSA for the abdominal aorta showing tight proximal stenosis of the right renal artery (arrowhead). (b) Post-angioplasty IA-DSA showing only mild residual stenosis (arrowhead). The trans-stenotic pressure gradient fell from 110 to 14 mmHg after angioplasty and the patient's diastolic pressure became normal. (c) IV-DSA for the abdominal aorta 5.5 months later. At this time the patient re-developed hypertension (180/120 mmHg). There is re-stenosis at the previous PTA site (arrowhead). (d) IA-DSA after repeat PTA. There was a trans-stenotic pressure gradient of 75 mmHg, which became zero after angioplasty. Note that the arterial lumen is now normal. The patient's blood pressure also became normal.

6 weeks and then every 6 months with blood pressure and medication evaluation.

Results

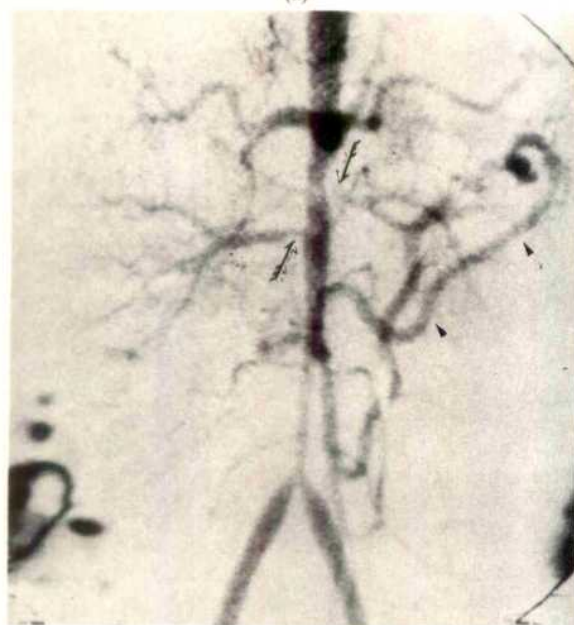
There were 21 female and 11 male patients with ages ranging between 18 months and 16 years (mean age 10.8 years). The clinical features are summarized in Table II. Constitutional symptoms, including fever and raised ESR, suggesting active disease were present in six children. A total of 36 DSA and two conventional angiograms were performed (Table III). The angiographic

features are summarized in Table IV and Figs 1–5. Obstructive lesions were common and usually involved the abdominal aorta (24 patients, 75%) and renal arteries (20 patients, 62.5%) (Figs 1–4). Aneurysms were uncommon (15.6%) (Fig. 6), were usually small and of saccular variety in three patients and of fusiform variety in two patients. All the patients with aneurysm formation had uncontrolled hypertension at the time of diagnosis. In contrast, hypertension was present in 70% of the remaining patients.

The pulmonary arteries were studied by IV-DSA in 20



(a)



(b)

Figure 3. (a) IV-DSA for the aortic arch in the LAO view showing mild narrowing of the aortic arch and occlusions of the left carotid and left subclavian arteries. (b) IV-DSA for the abdominal aorta in the AP view showing a long segment diffuse narrowing of the whole of the abdominal aorta. The visceral branches arise from the diseased segment of abdominal aorta. Both renal arteries (arrows) show proximal disease, the superior mesenteric artery is blocked and the artery of Drummond (arrowhead) is present. Both common iliac arteries are also diseased at origin.

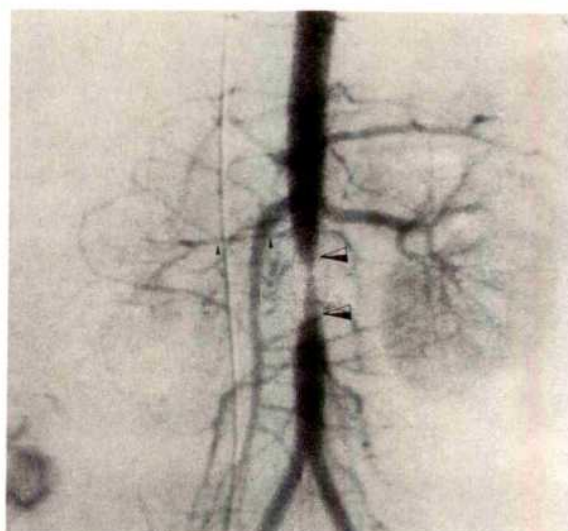


Figure 4. IV-DSA of the abdominal aorta in the AP view showing a long segment diffuse narrowing of the right renal artery (small arrowheads) and a short segment tight narrowing of the infrarenal segment of the abdominal aorta (open arrowheads).

patients and were involved in five patients (25%) (Fig. 7). The right lung was involved in two patients and involvement was bilateral in the remaining three patients. The upper zones were involved in all patients, either alone or in combination with other parts of lung. None of the patients with abnormal pulmonary arteries had any symptoms or signs related to pulmonary involvement.

Transluminal angioplasty was performed in eight patients (nine proximally located renal artery stenoses in seven patients and abdominal aortic stenosis in one patient). Two patients underwent two angioplasties each, one for recurrence of right renal artery stenosis 5.5 months after initial successful PTA and the second for bilateral renal artery stenosis. Initial success was obtained in eight out of 10 procedures (80%) (Figs 1 and 2). Percutaneous transluminal angioplasty resulted in clinical "cure" in one patient, "improvement" in five patients and "failed" in two patients. The mean diastolic blood pressure before PTA was 113.8 mmHg and after PTA was 91.3 mmHg. The follow-up period ranged between 5 and 16 months (mean 9 months). Recurrence was detected in one patient 5.5 months after initial success and this lesion was successfully re-dilated (Fig. 2). The two technical failures occurred owing to inability to cross tight proximal renal artery stenoses. There was associated narrowing of the juxta-renal segment of the abdominal aorta in both these patients, making catheter manipulation difficult.

Discussion

Takayasu's arteritis has been documented infrequently in children and we found only one previous

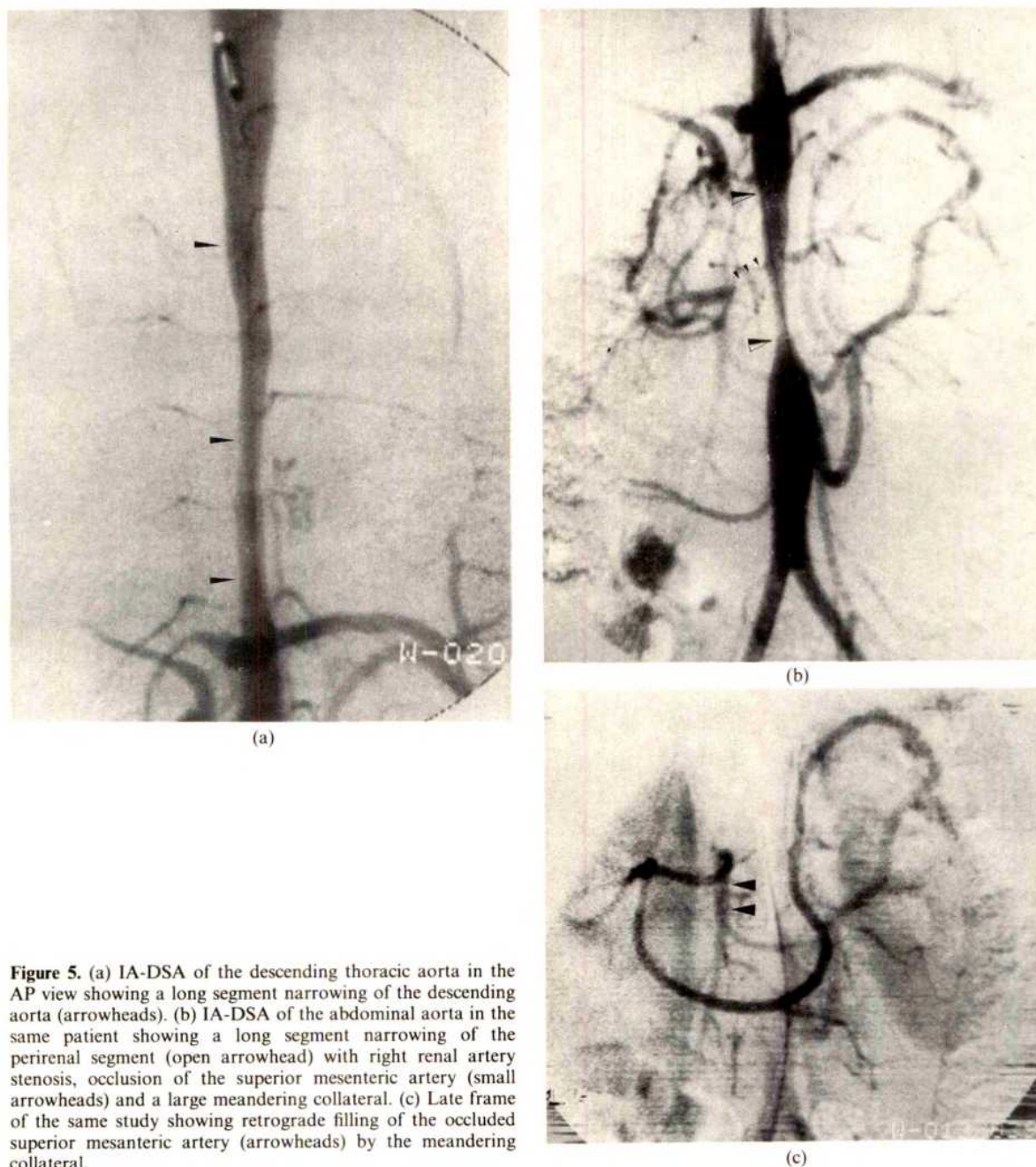


Figure 5. (a) IA-DSA of the descending thoracic aorta in the AP view showing a long segment narrowing of the descending aorta (arrowheads). (b) IA-DSA of the abdominal aorta in the same patient showing a long segment narrowing of the perirenal segment (open arrowhead) with right renal artery stenosis, occlusion of the superior mesenteric artery (small arrowheads) and a large meandering collateral. (c) Late frame of the same study showing retrograde filling of the occluded superior mesenteric artery (arrowheads) by the meandering collateral.

study (Golding et al, 1977), which reported arteriographic findings in 18 children less than 14 years in age. There were 10 females and the youngest child was 4 years old. The most common presenting feature was cardiac failure, always associated with hypertension, usually due to renal artery stenosis. Obstructive lesions were the most common (41 lesions) and were usually symptomatic. Aneurysms were less common (nine lesions) and were usually silent. The number of patients

showing stenotic lesions and aneurysm formation was not mentioned. The abdominal aorta was most frequently involved (14 patients) followed by the descending thoracic aorta (11 patients). The renal artery (10 patients) and the subclavian artery (five patients) were the most frequently involved branches of the aorta. Pulmonary artery involvement was not commented on.

The present study, involving 32 children, showed a definite female preponderance with a mean age at diag-

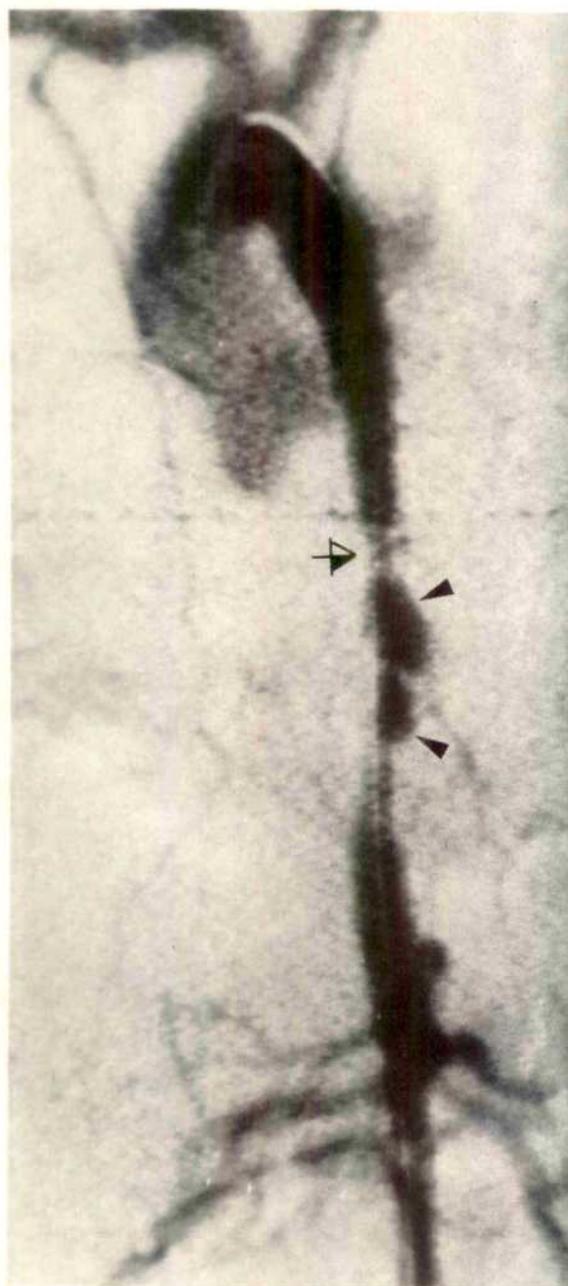


Figure 6. IA-DSA of the aortic arch in the left anterior oblique view showing stenosis (arrow) and small saccular aneurysms (arrowheads) in the descending thoracic aorta.

nosis of 10.8 years. Hypertension, diminished arterial pulses and bruits were the most frequently encountered clinical features. Congestive cardiac failure was present in 12 patients. All patients had more than one obstructive lesion, usually involving the abdominal aorta and renal arteries. Aneurysm formation was uncommon, usually small, predominantly involving the descending

thoracic aorta, and clinically silent. Pulmonary arterial involvement was seen in only 25% of patients. We may have underestimated the frequency of pulmonary involvement since only IV-DSA studies were performed to study pulmonary artery anatomy. Stenotic, non-occlusive lesions in the peripheral pulmonary artery may have been missed by IV-DSA. However, pulmonary DSA and radionuclide lung scans have recently been compared in the same patient and have shown an excellent correlation (Oudkerk et al, 1990).

Panaorto-arteriography in the diagnostic evaluation of these children has not been previously reported. The advantages and limitations of DSA in the diagnostic evaluation of adult patients have been reported previously (Yamamoto et al, 1987; Matsunaga et al, 1987; Sharma et al, 1989). Children differ from the adults for many reasons. The often associated manifest or occult cardiac failure limits the usefulness of IV-DSA for demonstration of the arterial system. In addition, the presence of misregistration artefacts resulting from voluntary or involuntary motion further hampers the usefulness of DSA examinations. Very young children are unable to hold their breath or stay still for successful IV-DSA. Indeed, even IA-DSA is sometimes compromised because of motion artefacts. In the present study, these limitations accounted for eight initially unsuccessful DSA examinations (six IV-DSA and two IA-DSA). In comparison, 89% of IV-DSA examinations in a previous study including adult patients were diagnostically adequate (Sharma et al, 1989). Whereas total contrast medium load can be a limiting factor in the adults owing to total number of runs needed for studying the complete arterial anatomy, smaller body surface area in the children allows examination of large areas of arterial anatomy in a single run. The whole of the thoracic aorta and its branches or the abdominal aorta and pelvic vessels can be frequently studied in one run, decreasing the total number of runs required for complete evaluation and the contrast medium load, the total dose of which was not a limiting factor in any examination in the present study.

The place of PTA in the management of arterial stenoses in Takayasu's arteritis is yet to be established. A few authors have reported the initial results of PTA (Saddekni et al, 1980; Hodgkins & Dutton, 1982; Hiramatsu et al, 1983; Dong et al, 1987; Khalilullah et al, 1988; Gu et al, 1988; Staller & Maleki, 1989; Park et al, 1989). Most of these relate to adult patients and the average age in two relatively large series was 27 years and 17.3 years, respectively (Dong et al, 1987; Gu et al, 1988). The response of PTA to the lesions encountered in children has not been described. We performed PTA for 10 arterial stenoses in eight children and obtained initial success in eight lesions. The mean follow-up was 9 months and initial success was maintained in five out of six patients. The long-term follow-up of these patients is awaited.

We conclude that Takayasu's arteritis in children is not uncommon in the Indian sub-continent and usually presents with hypertension. Obstructive lesions are

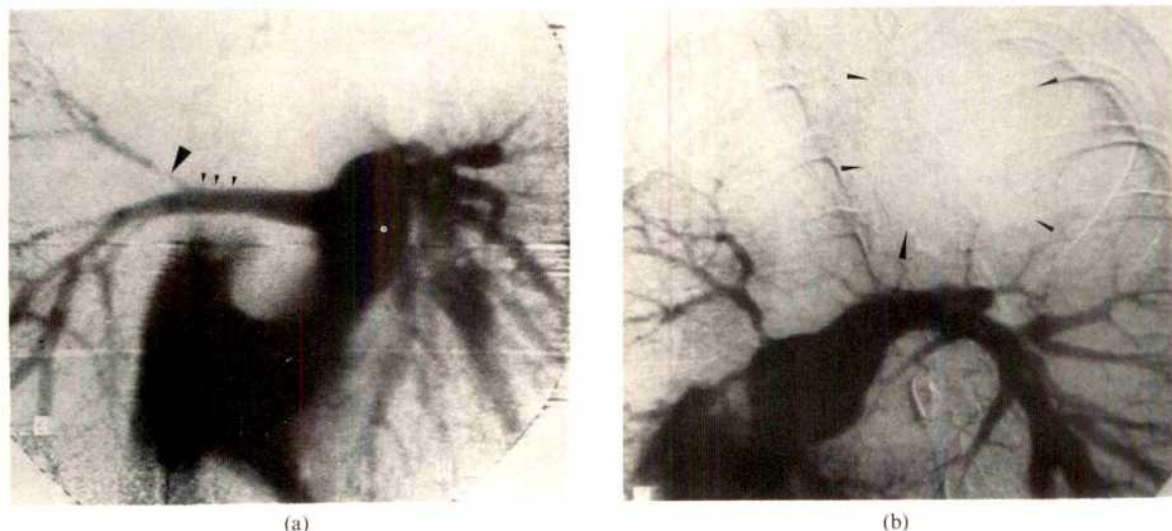


Figure 7. (a) IV-DSA for the pulmonary arteries in the AP view showing narrowing of the right main pulmonary artery (small arrowheads) and right upper lobe branch (large arrowheads). (b) LAO view in the same patient showing absence of filling in the left upper zone (arrowheads) with no demonstration of the left upper lobe branch. The narrowing of the right upper lobe branch is also seen.

always seen, commonly involving the abdominal aorta. In comparison, aneurysm formation is uncommon and occurs predominantly in the descending thoracic aorta. The renal artery is the most commonly involved branch of the aorta. In addition, pulmonary artery involvement is seen in at least 25% of patients. Whereas obstructive systemic arterial lesions frequently produce symptoms, arterial aneurysms and pulmonary arterial abnormalities are clinically "silent". Digital subtraction angiography (initial IV followed, if necessary, by IA) is usually adequate for establishing the diagnosis and planning the management. The preliminary results of PTA in these children show encouraging results but further long-term follow-up is needed before its efficacy in the management of stenotic lesions is established.

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A new coaxial needle for pre-operative localization of breast abnormalities

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Abstract. A new coaxial needle, containing a retractable anchoring wire with a helical tip, has been developed for purposes of mammographic and sonographic localization of non-palpable suspicious breast abnormalities before surgical excision. The helically shaped tip provides the needle with a number of potential advantages over other currently available localization needles. During *in vitro* comparisons with other needles quantitative and qualitative evidence was obtained to suggest that the new needle can be expected to have improved anchoring capability, be deflected less by tough fibrous tissue interfaces and be more visible sonographically. The anchoring wire can also be retracted and repositioned. Preliminary clinical experience with the needle was consistent with these expectations.

The increase in women undergoing mammography for detection of asymptomatic non-palpable breast carcinoma has been beneficial in reducing mortality (Baker, 1982; Tabar et al, 1985), but has resulted in a rise in the number of pre-operative breast localizations for suspicious lesions (Meyer et al, 1984; Ciatto et al, 1987; Rosenberg et al, 1987). Another recent trend is that sonographic imaging has become increasingly important in breast examination, sometimes being used for pre-operative localization of suspicious lesions (Jellins & Kobayashi, 1983; Egan & Egan, 1984; Guyer & Dewbury, 1987; Hackeloer et al, 1989). There are times when ultrasound can provide the surgeon with more specific localization of an abnormality; on those occasions when a lesion is demonstrated more clearly on ultrasound than by mammography and when ultrasound shows the abnormality but the mammogram is negative.

Many devices have been used for pre-operative localization of breast abnormalities including simple hypodermic needles, the injection of small quantities of various dyes, and needles designed specifically for the purpose—the majority of which are coaxial (Horns & Arndt, 1976; Kopans & Deluca, 1980; Kopans et al, 1984; Homer, 1985; Urrutia et al, 1988; Ueno et al, 1989). Both mammography and sonography have been used to guide the positioning of such devices, depending on the nature of the abnormality and the particular expertise and preference of the radiologist.

Mammography is, however, by far the most common method for localizing breast lesions and the technique of stereotactic positioning of the needle is becoming increasingly common.

Each of the above devices possess disadvantages. It would appear that the dye injection method is a successful approach if diffusion of the dye through the breast tissue is minimized, by injecting only a small amount of dye, and by proceeding as rapidly as possible to surgery. Straight needles are not anchored within the breast parenchyma, making it possible for them to move out of position before surgery takes place. This shortcoming stimulated the development of specialized needles, each of which contains a coaxial inner anchoring wire. The configuration of the tip of the anchoring wire, after it has emerged from the insertion needle, is the principal factor which determines the differences between one design and another. However, with current systems there remains a theoretical possibility that needle migration between the time of introduction and surgery may still occasionally take place. Furthermore, only some of the systems permit retraction and re-positioning of the anchoring wire. In the presence of tough fibrous tissue we have occasionally found difficulty in making the anchoring wires of some types of needle systems either penetrate the tissue, particularly with the retractable types of needle, or remain fixed within it.

When using ultrasound for localization, correct positioning of the anchoring wire is made difficult because of the poor sonographic visibility of currently available needle tips. In general, they are only visible because it is possible to see on a real-time sonographic display the appearance and disappearance or the movement of the

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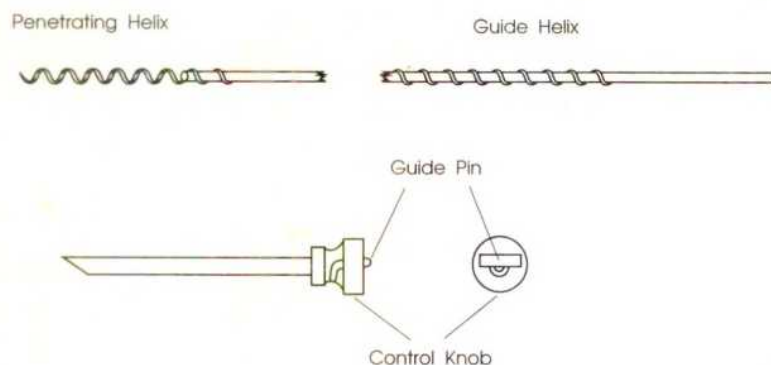


Figure 1. Component parts of the double helix breast localization needle. The length of the anchoring wire from the proximal part of the penetrating helix to the proximal part of the guide helix is equal to the length of the insertion needle.

echo from the needle tip or anchoring wire when either the needle or the ultrasound probe are moved. Furthermore, because of this difficulty, radiologists may be discouraged from using ultrasound guidance when a mass is demonstrated better by sonography than by mammography.

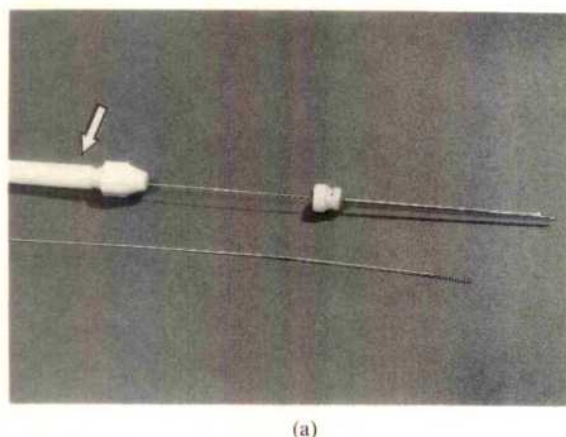
We have designed and developed a new coaxial needle for breast localization purposes to overcome some of the deficiencies of present systems. The main operative feature is the helical configuration to the tip of the anchoring wire. Once the outer insertion needle is at the correct position the anchoring wire may literally be screwed into the tissue, or unscrewed if necessary. This paper provides a description of (a) the needle, (b) *in vitro* experiments comparing some of its properties with those of other commonly used needles, and (c) initial clinical experience in using the needle.

Materials and methods

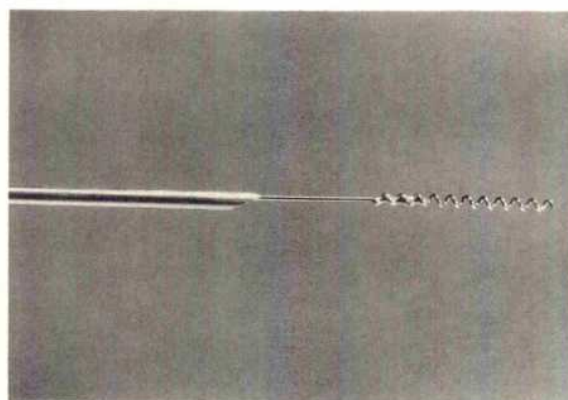
Instrumentation

The breast localization needle is shown in Figs 1 and 2. It consists of a thin stainless steel wire with a helix of the same material, 1 cm in length, welded to one end. A

second helix, of exactly the same length and pitch as the first, is wound around and welded to the centre section of the shaft, such that the distance from the tip of the end helix to the beginning of the second helix is equal to the overall length of the insertion needle. The insertion needle is also made of stainless steel and has a controlling knob at one end, across which is mounted a stainless steel wire. The wire presses firmly on the shaft when it is in the lumen of the needle, serving first as a nut on the thread of the helix and secondly as a guide to allow the radiologist to know exactly how far the helix at the tip of the needle has been screwed into the tissue. After confirming that the anchoring wire has been correctly placed both it and the insertion needle are kept in place whilst the woman is taken to surgery. A principal advantage of not removing the insertion needle is that it provides the surgeon with a more easily palpable track towards the lesion (Homer, 1988). It is also less easy to transect accidentally than is the anchoring wire alone. In some hospitals removal of the insertion needle is preferred, in which case it is possible for the surgeon to pass a cannula over the guide wire immediately before exploration.



(a)



(b)

Figure 2. (a) The double helix coaxial needle system fully assembled (above) and an additional anchoring wire (below). The pin vice (arrow) grips the anchoring wire, permitting it to be manually twisted so as to screw the penetrating helix into the tissue. (b) Close up view of the penetrating helix with the insertion needle partially removed.

For the laboratory studies described below the prototype models of our helix needle system were manufactured using 18 gauge insertion needles. For the clinical studies 20 gauge needles were used on eight of the patients and 18 gauge needles on the remainder.

In vitro experiments

In vitro studies were performed to provide a preliminary comparison between the properties of the new "double helix" needle and those of three currently available breast localization needles. The three other needles used were the Homer-Mammalok (manufactured by Namic, Glens Falls, New York 12801, USA), the Kopans Spring Hook Localizer (manufactured by Cook Inc., P.O. Box 489, Bloomington, Indiana 47402, USA) and the Percuguide I (manufactured by E-Z-EM Inc., Westbury, New York 11590, USA). The experiments were designed for simplicity and to provide comparisons of anchoring capability, ability to localize accurately and embed within the breast tissue, and sonographic visibility.

Seventeen fresh mastectomy specimens were used; the time between excision of the breast specimens and their use ranged from 30 min to 2 h. Thirteen specimens were used to test the anchoring properties of the needle systems (eight for measuring the degree of migration when pulled by a constant force and five for measuring the force needed to extract completely the needles) and four were used to assess the capabilities of the anchoring wires to embed themselves, at the desired location, within the breast tissue. We have termed the latter experiments "re-configuration studies", since the needle systems are designed so that as the anchoring tip emerges or is unsheathed from the insertion needle it re-configures its shape, with the function of embedding and immobilizing itself within the tissue. In the case of the Helix and Homer needles the tip is embedded by advancing it beyond the outer needle. For the Kopans needle and the Percuguide, which are non-retractable systems, the barbed anchoring wire is embedded when the outer needle is withdrawn about 1 cm while keeping the inner wire stationary. Whatever the technique, if complete re-configuration of the tip has not taken place in practice, the needle may not be firmly in position and may be liable to migration if pulled. In the results to be reported in the next section (Tables I, II & III) a completely new needle was used to generate each set of data. All needles were inserted to a standard depth of 3.5 cm, aiming to localize a specific but independent region of the specimen with each needle. In the migration and re-configuration studies the breast tissue regions, into which the needles were inserted, were classified as either fibrous or fatty and equal numbers of regions of each type were tested. No such distinction was made in the five specimens used for the complete extraction studies, although in all cases the breast tissue was judged by a pathologist to be composed of at least 60% fibrous tissue and less than 40% fat.

Anchoring capability was assessed after localization, firstly in terms of the degree of migration that occurred

when a constant extraction force was applied to the needle for a fixed time period and, secondly, according to the relative force needed to remove completely the needle from the breast. The forces used to pull on the needles and the times for which they were applied (given below) were quite different from those which one might expect to encounter clinically. For example, during the time between localization and surgery the wire and/or needle might inadvertently receive a number of momentary sharp knocks or pulls. However, this situation would be difficult to simulate experimentally and the repeatability of the results would be poor. For this initial study relatively large forces and long pulling times were chosen to maximize our ability to demonstrate the differences between the needles, if any, owing to their design. A thorough and long term clinical evaluation would still be required to discover whether any differences between needles, demonstrated in such experiments, resulted in a significant difference in the number of migrations when used in clinical practice.

For the migration studies, balance weights were suspended from a length of ligature. The ligature was passed around a pulley and was clamped to the shaft of the needle by a small pin vice. This allowed the vertical pull of the weight to be translated into a horizontal pull on the needle, so that the tissue sample could be placed in a specimen X-ray box for direct observation of the position of the needle tip. In the complete extraction studies, the tissue was held down by a Perspex plate with a hole in it, through which the needle passed as it was pulled vertically upwards by the ligature. The ligature passed over a pulley fixed to a horizontal aluminium bar, continued horizontally to a second pulley and then downward to a spool on a geared-down electric motor. The motor was turned on and a chart recorder was used to monitor continuously the signal from a strain gauge, which was fixed to the aluminium bar with epoxy cement and had been calibrated in terms of force using gram weights.

Two types of migration study were performed. In the first, the initial response of the needle was studied by measuring the change in the position of its tip after 10 s of pulling with a 20 g weight. In the second, the same force was applied for 45 min. The initial and final position of each of the needles was obtained from specimen radiographs after the weight had been removed and the tissue had been allowed to relax back into its unstressed position.

In the re-configuration studies specimen radiographs, taken after the needle had been placed in position, were used to decide whether the tip of the needle had been successfully embedded at the desired location. Visual assessments were made as to whether the tip re-configuration was complete or incomplete.

Sonographic visibility was compared by imaging the needles within mastectomy specimens and preserved (formalin-fixed) cat livers using an Acuson 128 ultrasonic scanner operating at 7 MHz with a 38 mm linear array (hand held) transducer—this being the system used routinely in our hospital for ultrasonic breast

Table I. Anchoring characteristics of the four needles. Figures are given for the average distance migrated in excised breast tissue when the needle was subjected to a constant extraction force due to the weight of a 20 g mass, for the stated time. n is the number of needles used of each type and the SD values given are for (σ_{n-1})

Total pulling time	Needle	Migration distance (mm)			
		Fibrous tissue ($n=6$)		Fatty tissue ($n=6$)	
		Mean	SD	Mean	SD
10 s	Homer	1.2	0.3	2.7	0.7
	Percuguide	5.0	0.3	6.8	0.8
	Kopans	0.9	0.1	1.0	0.2
	Helix	0.3	0.2	0.8	0.2
45 min	Homer	3.2	0.7	3.3	0.5
	Percuguide	7.5	0.6	10.3	0.4
	Kopans	1.5	0.4	2.3	0.7
	Helix	1.0	0.7	1.6	1.2

Table II. Anchoring characteristics of the four needles. For each of the five tests of each needle type, values are given for the relative force necessary to completely remove the needle from excised breast tissue

Needle	Relative force (g weight)					Mean	SD
	Test 1	Test 2	Test 3	Test 4	Test 5		
Homer	480	230	230	140	290	274	114
Percuguide	680	540	380	803	520	585	145
Kopans	300	420	510	260	780	454	185
Helix	900	1220	900	900	1100	1004	132

examination. The images were evaluated in real-time and used to judge both the ease of identification of the anchoring wire and the ability to specify the location of its tip in the tissues examined. Although increased visibility of the guide wire would not be expected to aid needle guidance during insertion, it should improve ability to confirm and document correct placement. The rationale for choice of specimens was similar to that for the anchoring studies, *i.e.* to provide an initial experimental situation within which it would be simple to demonstrate differences between needles. The cat livers provided a uniform low-level echo background, giving all needles the chance for maximum visibility and the opportunity to study the echo structure of the tips of the

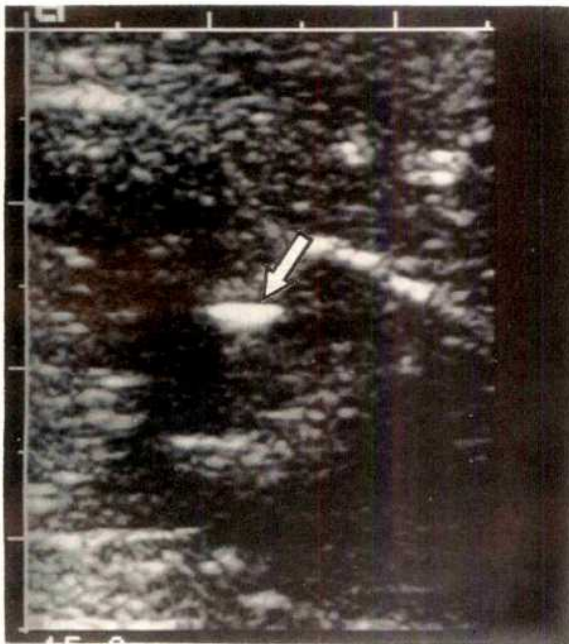
anchoring wires under close to "ideal" imaging conditions. The mastectomy specimens provided a realistic breast echo background but still a controlled situation within which to compare the appearances of the needles.

Clinical studies

Initial clinical experience with the new needle has included 17 patients to date. Eleven of the abnormalities were localized using mammography. In each of these cases there was no palpable abnormality. Microcalcification alone was present in three cases, a mass in five and microcalcification associated with a mass in three cases. Six of the overall 17 cases were localized solely by ultrasound guidance. Each of these six cases

Table III. Re-configuration and deflection studies. Twelve tests in excised breast specimens were performed on each type of needle. The re-configuration of the anchor tip was judged either complete or incomplete and the final position of the tip was judged as either having deflected from the desired location or not deflected

Needle	Number where re-configuration was judged complete		Number where tip had stayed at the desired location (<i>i.e.</i> not deflected)	
	Fibrous ($n=6$)	Fatty ($n=6$)	Fibrous ($n=6$)	Fatty ($n=12$)
Homer	1 (17%)	4 (67%)	0 (0%)	5 (83%)
Percuguide	1 (17%)	3 (50%)	1 (17%)	4 (67%)
Kopans	3 (50%)	6 (100%)	5 (83%)	6 (100%)
Helix	6 (100%)	6 (100%)	6 (100%)	6 (100%)



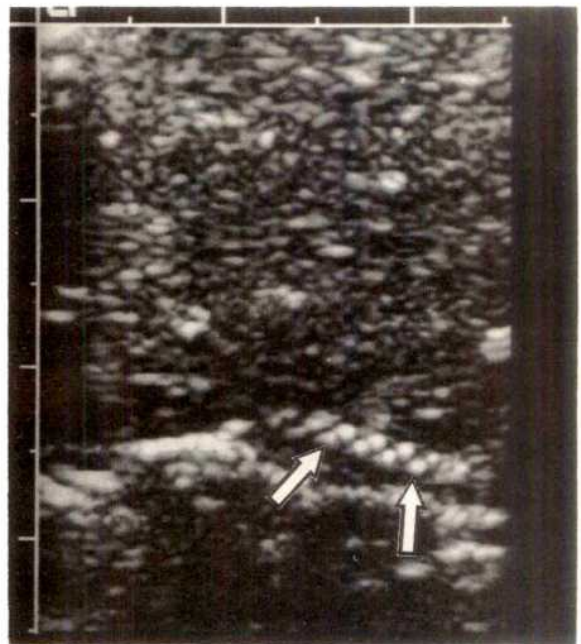
(a)



(b)



(c)



(d)

Figure 3. Examples of the plain film (static) sonographic appearances of the various needles embedded in formalin-fixed cat livers. In each of the images the echo structure corresponding to the needle tip (originally identified in real-time) is indicated by an arrow. (a) Homer, (b) Percuguide, (c) Kopans, (d) helix.

had non-specific clinically palpable nodularity and segments of thickening within both breasts. They included one perilobular haemangioma, two infiltrating ductal carcinoma, one lobular carcinoma *in situ* and

three cases of mastopathy. In four of these cases the abnormality was appreciated only by ultrasound. In the other two, there were areas of relatively diffuse architectural distortion on the mammogram where sonography

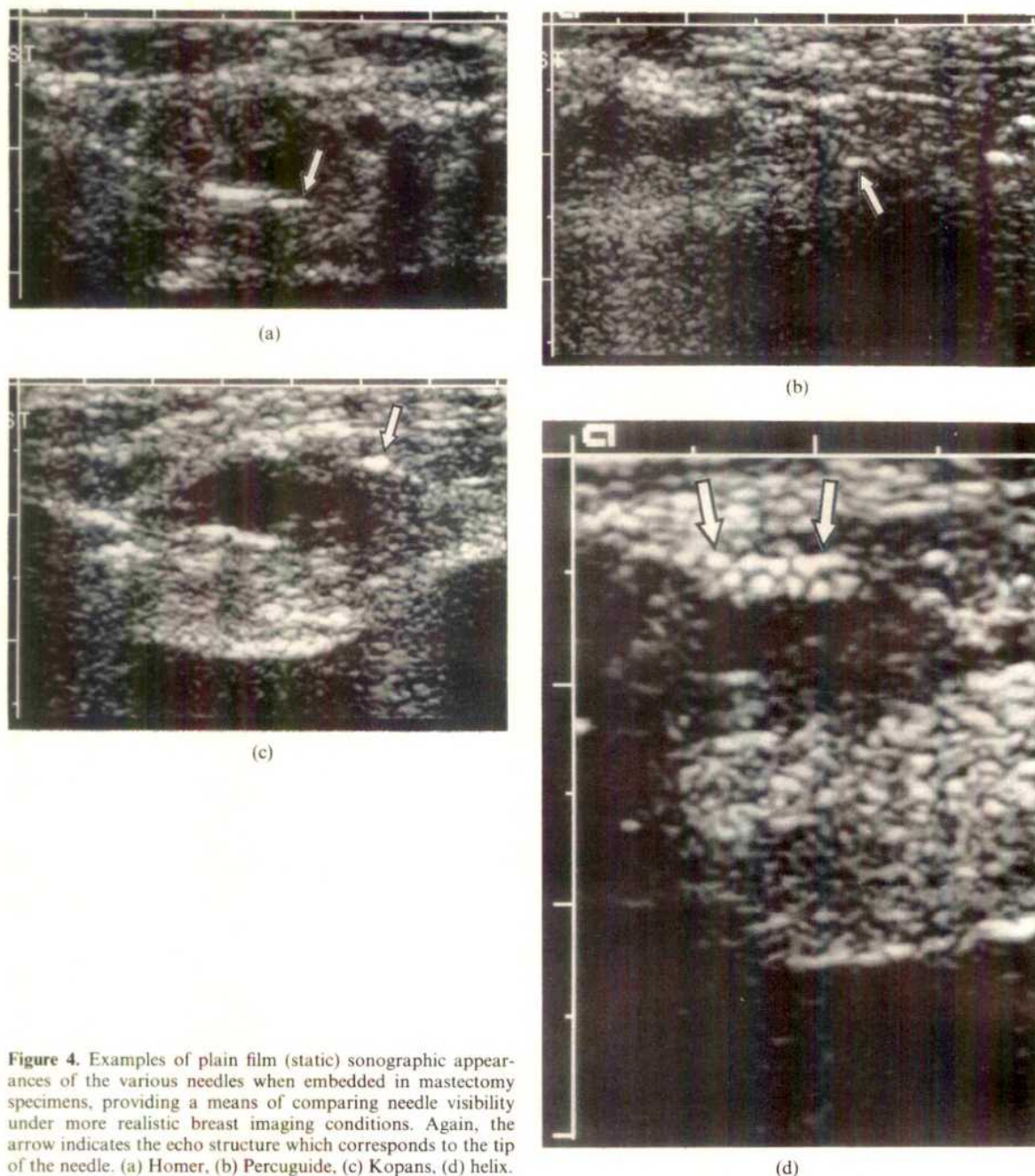


Figure 4. Examples of plain film (static) sonographic appearances of the various needles when embedded in mastectomy specimens, providing a means of comparing needle visibility under more realistic breast imaging conditions. Again, the arrow indicates the echo structure which corresponds to the tip of the needle. (a) Homer, (b) Percuguide, (c) Kopans, (d) helix.

provided a more accurate method of pinpointing the area of abnormality.

The mammographic localization sites were selected by use of geometrical measurements obtained from the cranio-caudal and medio-lateral radiographs, or by employment of the biopsy compression device as attached to the mammography unit. The sonographic localizations were performed by observation of the needle tip as it was inserted in real-time using a hand

held 7 MHz linear array transducer. Using standard aseptic technique and local anaesthesia in all cases, the entry needle was inserted to the location of the tissue targeted for subsequent biopsy. The distal helix at the tip of the anchoring wire was then screwed into the tissue by turning the proximal part of the anchoring wire, which includes the identical reference helix, with the aid of the pin vice indicated in Fig. 1. Subsequent confirmation of correct localization was obtained by



Figure 5. Mammographic localization of a well differentiated intraductal carcinoma demonstrating the plain radiographic appearance of the helix needle (cranio-caudal view).

repeat mammography and/or sonography, as appropriate to each case.

Results

The double helix needle displayed better anchoring characteristics than any of the other needles tested, whether embedded in fibrous or fatty breast tissue. Of all the needles it migrated the least, when subjected to a constant extraction force, for both short and long time periods and required the greatest force to remove it completely from the tissue specimens (Tables I & II). In the latter study (Table II) there was little to distinguish the performances of the other needles, but the average force required to remove the double helix needle from the breast specimens was greater than that for the best of the others by more than 3 SD about the mean.

The re-configuration studies also showed comparatively superior performance by the helix needle (Table III). This was particularly noticeable when the needles were placed in tough fibrous breast tissue, where the tips of many of the anchoring devices would often (a) not fully reform beyond the outer cannula and (b) deflect away from the intended location once unsheathed. No difficulty was encountered with the helix tip, since by design it is not required to change shape when it emerges from the cannula and the mechanics of the way in which it is used, as a screw, almost eliminate the possibility of deflection. Placement of the helix tip within 5 mm or less of the desired position was obtained in every case.

Comparative examination of the real-time sonographic appearances of the localization needles demonstrated that the tip of the helix needle had a repeatable and easily identifiable form or "image signature", whereas the tips of the other needles were difficult to see against background tissues and their position could not usually be specified accurately on the hardcopy plain images. Examples of the typical ultrasonic appearances of each of the needle tips within the cat livers are provided in Fig. 3, and within the mastectomy specimens in Fig. 4.

To date, the preliminary clinical studies have needed only a single localization attempt, with no need to reposition the needle by the radiologist. During very early tests with pieces of excised tissue it was noted that it was possible to reposition the helix needle by unscrewing the tip back into the outer cannula and starting again. In each case the tip of the needle was placed within 1 cm of the targeted area. No technical problems or complications were encountered and no dislodgements occurred. Pre-operatively targeted lesions were removed in all cases, as confirmed by specimen radiography, histology or repeat sonographic examination of the patient. Examples of the *in vivo* mammographic and sonographic appearances of the helix needle are provided in Figs 5 and 6. In both cases the images displayed were used in documenting the localization concerned.

Discussion

The new breast localization needle is termed the "double helix" needle, in view of its design characteristics. It allows the helix at the tip of the anchoring wire to be screwed into the target breast tissue in an identical manner to the visible proximal helix. The overall improved anchoring capability of the needle, as demonstrated in the *in vitro* testing, is of potential importance because it may reduce the chance of a position change during the time between localization and excision. Such position changes were sometimes a problem in routine use of many existing breast localization needles and represented the motivation for developing the double helix needle.

The superior re-configuration properties of the double helix needle, also demonstrated by the *in vitro* experiments, are felt to be of potential importance for similar reasons. If a needle tip is believed to be properly re-configured and embedded in the tissue, but in fact it is not, then it will be even more susceptible to position changes than the above anchoring studies suggest. All of the anchoring studies were performed having previously confirmed that re-configuration had taken place.

During the *in vitro* experiments the forces applied to pull on the needles were much larger than any needle is likely to experience in clinical practice. This was done to permit the rapid demonstration of any major differences between the different needles, without the need for extensive experiments involving large numbers of specimens. Given the fact that deficiencies had already been observed in existing needle designs during clinical use, it was felt that such comparative experiments, although conducted under somewhat artificial circumstances, were valuable as a means of determining whether or not our design objectives had been met. Following the encouraging results of the early clinical tests, a substantial and statistically unbiased clinical trial is now required to evaluate further needle migration with the double helix needle.

The sonographically identifiable tip of the anchoring wire offers a greater opportunity for confirmation and documentation of accurate positioning of the needle,

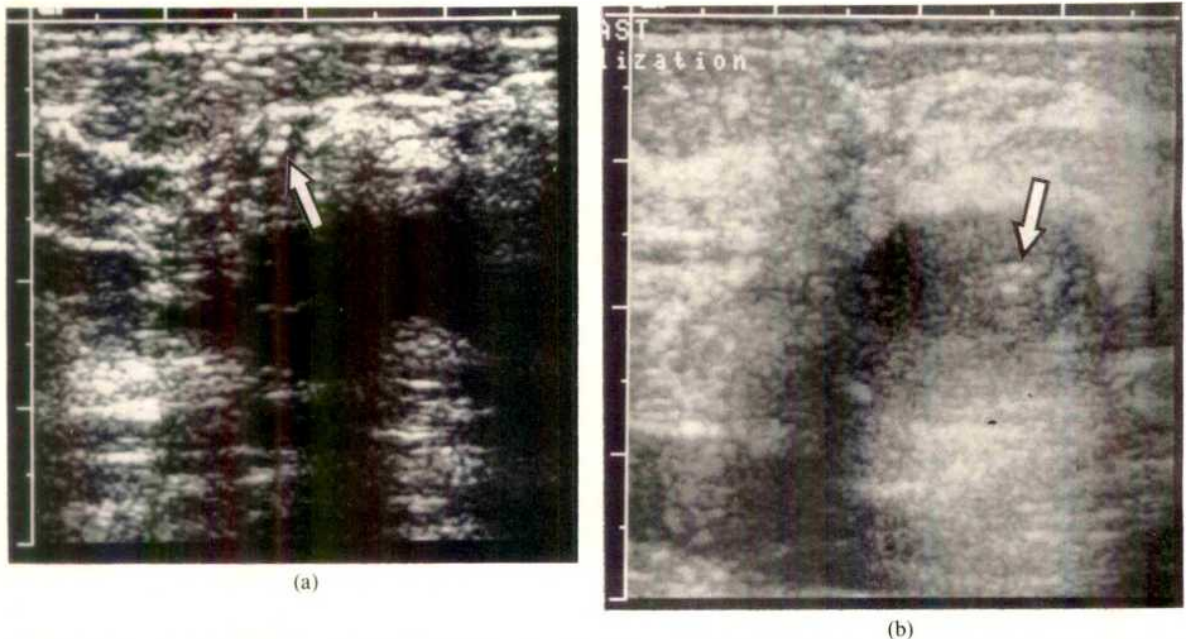


Figure 6. Examples of localization of the helix needle by sonography in two different patients, each with normal mammography. In (a) the tip of the anchoring wire is adjacent to the lesion, a biopsy-proven atypical papillomatosis and perilobular haemangioma. In (b) the tip of the anchoring wire is embedded within a lobular carcinoma.

particularly when the target lesion is better demonstrated using ultrasound rather than mammography. Although the improved sonographic visibility of the needle relative to the other needles was initially demonstrated *in vitro* using mastectomy specimens and formalin-fixed cat livers, the property of excellent visibility of the helix tip was maintained in the clinical studies, making the radiologist's task easier than when using other needles. It may be noted that all masses localized solely by ultrasound resulted, as with those localized by mammography, in a successful positive biopsy.

One possible disadvantage of the helix needle system could be that the presence of the second external helix might prevent the wire being pulled forward through the operative site from a skin incision which is at a position different from where the needle enters the breast. This would never be a problem in our institution, where the needle is always positioned via the shortest route to the skin surface. If two different approaches are required then two needles are placed. It may also be of interest to know whether one needle system results in any greater amount of bleeding than the others. This has not been the subject of specific study, but in the present work no excessive or unusual haematoma was noted either by the surgeon or by the pathologist. Finally, some workers may prefer not to leave the outer needle in the breast when the patient is sent to surgery. Although we routinely leave the needle in place it is quite possible, if the time between localization and surgery is likely to be long, to remove it so that the wire can be taped to the skin surface.

Since the double helix needle is not currently available from a commercial source we are not able to state its cost, but no special fabrication problems are anticipated which would make it substantially more expensive than other localization needles.

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Embolization with steel coils using a saline flush technique

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Abstract. A method using saline flush to push Gianturco steel coils through catheters is described, and has been successfully used in 45 patients. The saline flush technique requires no precise matching of coils and catheters, solves problems associated with the conventional method and simplifies the coil embolization procedure.

Gianturco stainless steel coils are widely used for transcatheter intravascular occlusive therapy. The conventional steel coil insertion method uses a guidewire as a pusher. Recently, the Cook Inc. technical data for straight Hilal coils have mentioned the saline flush technique. This report introduces and discusses a method of saline flushing to push conventional steel coils.

Materials and methods

Patients, coils and catheters

Since December 1988, we have performed therapeutic arterial coil embolization using a saline flush technique in 45 patients (Table I). Surgical gelatin (Gelfoam) was used with coils for management of bleeding cases. Fifty-seven vessels were embolized (Table II). We used a total of 100 coils: 57 were 025-2.5-2 (0.025 inch diameter, 2.5 cm long, 2 mm helical diameter) type and 43 were 038-4-3 type of coils (Cook Inc.). We used 3.5F (0.025 inch inner diameter) or 5F (0.038-0.049 inch inner diameter) catheters of polyethylene or polyurethane. Both tapered-tip and non-tapered-tip catheters were used. No catheters with side-holes at the tip were used.

Table I. The use of steel coils in 45 patients

Indication	No. of patients
Arterial redistribution for intra-arterial infusion chemotherapy	31
Gastrointestinal bleeding	8
Haemoptysis	3
Urinary bleeding	2
Hepatic arterioportal shunt	1
Total	45

Table II. The arteries embolized

	Number
Gastroduodenal artery	25
Right gastric artery	13
Left gastric artery	2
Hepatic artery	1
Right hepatic artery	1
Replaced right hepatic artery from the superior mesenteric artery	2
Replaced left hepatic artery from the left gastric artery	2
Branch of the jejunal artery	3
Branch of the ileal artery	2
Branch of the right colic artery	1
Right bronchial artery	3
Branch of the right renal artery	1
Branch of internal iliac artery	1
Total	57

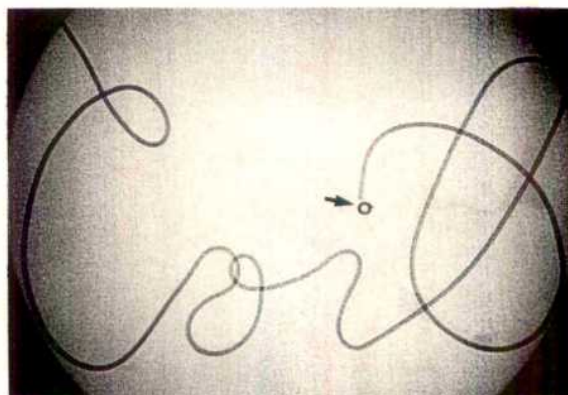
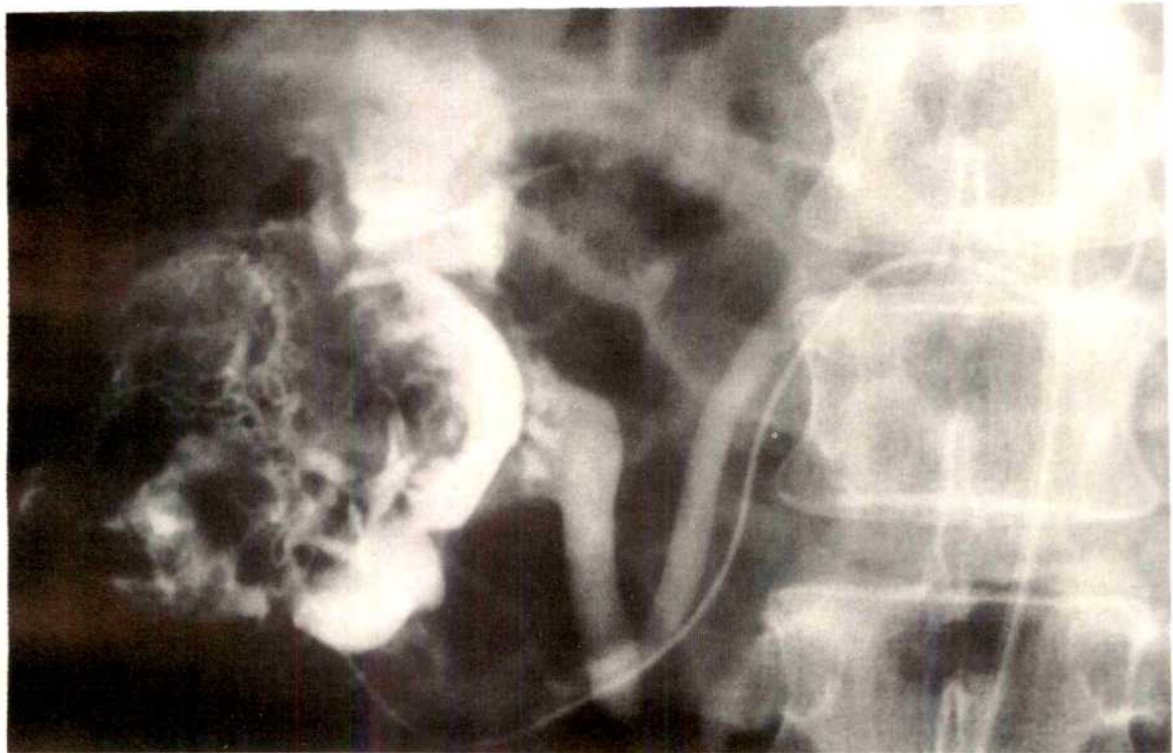


Figure 1. An experimental trial. A 038-4-3 coil (arrow) passed through the 0.049 inch inner diameter "coil" shaped catheter.



(a)



(b)

Figure 2. (a, b) Bleeding from a colon tumour. A 025-2.5-2 coil was flushed to the branch of the right colic artery (arrow).

Technique

It is important to maintain the catheter tip in the proper place at all times. The catheter tip should be checked for unwanted movement by making a strong hand injection of saline under fluoroscopic observation.

The coil is inserted into the catheter for about 5 cm with a guidewire. Under fluoroscopic observation, the coil is flushed with a syringe filled with saline. We prefer a 10 ml syringe but a smaller or larger one can be used effectively. The feeling is similar to that of performing a

hand injection of contrast medium in an angiogram. Care should be taken not to shoot the coils too strongly into the blood vessels. Saline flush can be repeated if necessary. A higher pressure is sometimes needed to flush the coil past a curve in the catheter.

In cases where the coil stops at the catheter tip, the catheter can be gently withdrawn while flushing with saline. If this is unsuccessful, the coil can be pushed out using a guidewire that matches the catheter.

Results

We successfully and accurately embolized the intended vessels using this method in all cases. There was no unwanted movement of the catheter tip when the coil was flushed out and there was no premature coiling in the catheter. No complication resulted. There was no need for catheter exchange to match catheter and coil. There were no advantages between different catheter materials. 025–2.5–2 coils were easily flushed, especially when relatively large 0.038–0.049 inch inner diameter catheters were used. Only three 038–4–3 coils required a final push out from the catheter tip using a guidewire.

Figure 1 shows an experiment in which we easily flushed a coil through a catheter in which we had shaped multiple bends. Figure 2 shows an illustrative case.

Discussion

Gianturco et al (1975), in the first report of mechanical occluding devices, introduced "cotton tails", small metallic segments with attached cotton threads, and "wool coils", the original stainless steel coils. Cotton tails were flushed out by saline injection. Chuang et al (1981) recommended the injection of 1–3 ml saline to disentangle bunched coil strands in the catheter. The Cook Inc. technical data for straight Hilal coils mention the saline flush technique. Saline injection as a method for 0.038 inch steel coil insertion has not yet been reported.

The conventional method requires the precise matching of coils, catheters, and guidewires (Chuang et al, 1980, 1981; Mazer & Martin, 1984), even though the proper catheter for the intended vessel is not always suitable for the coil size required for the vessel. When materials are not matched, the guidewire puts pressure on a single point of the coil, which sometimes results in wedging of the coil or in overlapping of the coil and the guidewire (Chuang et al, 1981; Mazer et al, 1984). Using this method, a 0.025 inch diameter coil cannot be inserted through commonly used diagnostic catheters of over 0.038 inch inner diameter. In changing catheters, spasm of the previously catheterized vessel may cause difficulties in recatheterizing. Another problem arises when placing coils of different diameters (0.025 inch and 0.038 inch), the previously placed coil interfering with

the advancement of the guidewire necessary for catheter exchange.

The technique of using saline flush does not require the precise matching of materials. No new materials or modifications (Mazer et al, 1984; Castaneda-Zuniga et al, 1980) are needed. No catheter exchange procedures are needed when injecting coils of different diameters, and even a standard diagnostic catheter is suitable for injection of most coils. A smaller coil can pass smoothly through a larger catheter without significant loss in saline volume, as low friction allows for faster movement of the coil through the catheter. Catheters with tip-side-holes, which may catch the coil or release saline pressure, should be avoided, however. There was no premature coiling in our cases even when the catheters did not match the coils. We believe this was because saline puts pressure over the entire coil rather than at a single point.

There were no complications in placing of 100 coils. Before clinical application, we made extensive trials with both matched and mismatched coils and catheters. All coils easily passed through the catheters using relatively low injection pressures and no jamming or wedging occurred. Both preclinical trials and clinical results show that this method is safe when performed by experienced interventional radiologists.

In conclusion, this method solves problems associated with the conventional method, simplifies the coil occlusion procedure, especially when placing small coils using relatively large catheters, and seems to be as safe as other interventional radiological techniques for steel coil embolization.

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Evaluation of $^{99}\text{Tc}^{\text{m}}$ Technegas ventilation scintigraphy in the diagnosis of pulmonary embolism

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Abstract. In the diagnosis of pulmonary embolism, perfusion lung scintigraphy offers high sensitivity but low specificity. The specificity can be significantly increased by the use of combined ventilation and perfusion studies. Most aspects of perfusion lung scintigraphy are uniformly accepted but the technique of ventilation imaging varies from centre to centre. This study describes a new technique for the performance of ventilation scintigraphy using a suspension of ultrafine carbon particles labelled with $^{99}\text{Tc}^{\text{m}}$ ("Technegas"). The technique combines the ready availability of $^{99}\text{Tc}^{\text{m}}$ and its optimal imaging properties with an easily administered radiopharmaceutical of particle size sufficiently small to deposit in the alveoli. Of 63 patients studied by conventional perfusion scintigraphy plus Technegas ventilation scintigraphy, images of diagnostic quality were obtained in all. 31 of these patients also had a ventilation study using $^{81}\text{Kr}^{\text{m}}$ gas and in only one instance did the two methods of ventilation imaging lead to differing interpretations. We conclude that high quality diagnostic images may be obtained using this new technique, which can be made available on both a routine and an emergency basis, thus improving the service provided for patients suspected of having pulmonary embolism.

Pulmonary embolism (PE) is a major cause of morbidity and mortality. It is estimated to account for approximately 21 000 deaths annually in England and Wales and over 200 000 in the USA (Dalen & Alpert, 1975). Treatment by anticoagulation is well tolerated in the majority of cases, but as it can sometimes be hazardous, a reliable means of diagnosis is essential. Whilst contrast medium pulmonary angiography (CPA) is generally regarded as the "gold standard" of definitive diagnosis it is an invasive procedure which carries a small but significant mortality (Dalen et al, 1971). Perfusion lung scintigraphy is a safe, non-invasive and highly sensitive technique. The imaging protocol using $^{99}\text{Tc}^{\text{m}}$ labelled macroaggregates ($^{99}\text{Tc}^{\text{m}}$ -MAA) or microspheres of albumin is well established, and although of low specificity the combined use of ventilation studies greatly increases the specificity whilst preserving the high sensitivity of the procedure.

The imaging protocol for ventilation scintigraphy varies depending upon the radiopharmaceutical used; this in turn is dependent upon the availability of equipment and clinical preference. ^{133}Xe gas has been used for clinical studies since 1970, is inexpensive and readily available but has less than optimal photon energy (80 keV) and a relatively long half-life (5.3 days). One alternative is ^{127}Xe , which has higher photon energy (172, 203 and 375 keV) and a longer half-life (36.3 days) but is expensive, and its higher energy results in poorer

resolution. The usual practice with these gases is to obtain wash-in, steady state/equilibrium and wash-out images in a single projection, although it is possible to obtain an additional wash-out image in an oblique or lateral projection.

$^{81}\text{Kr}^{\text{m}}$ gas has been available since the mid-1970s and is probably the most widely used radiopharmaceutical for ventilation imaging in the UK; it has a very short half-life (13 s) and can be continuously eluted from a ^{81}Rb generator (half-life, 4.7 h). The generator, being cyclotron produced, is expensive and availability depends, to some extent, on proximity to the cyclotron. It can, however, be used for several patients for both routine and emergency studies. $^{81}\text{Kr}^{\text{m}}$ has a photon energy of 190 keV and its short half-life enables multiple views in different projections to be obtained either before or after the perfusion study.

A variety of $^{99}\text{Tc}^{\text{m}}$ -labelled aerosols are also in current use. They have some advantages over the gases in that the inhalation technique may be easier and multiple views can be obtained. In addition, $^{99}\text{Tc}^{\text{m}}$ has optimal imaging properties and is readily available. Difficulties arise, however, in both the production and the delivery of the aerosol. Particles of less than about $2\text{ }\mu\text{m}$ are required to avoid central deposition and achieve peripheral airway penetration (Agnew, 1984). Deposition will also be dependent on the rate and depth of inhalation and it may not always be possible to standardize this in ill patients.

A new radiopharmaceutical for ventilation scintigraphy has been developed by William M. Burch and colleagues (Burch et al, 1986) in conjunction with Tetley Technologies Pty Ltd of Sydney, Australia. This radio-

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pharmaceutical, "Technegas", is an ultrafine dispersion of $^{99}\text{Tc}^{\text{m}}$ -labelled carbon particles which have a diameter of less than $0.2\ \mu\text{m}$ (Strong & Agnew, 1989). This is considerably smaller than any aerosol previously used for ventilation imaging and should therefore achieve peripheral airway penetration comparable with that produced by $^{81}\text{Kr}^{\text{m}}$ and ^{133}Xe . The purpose of this study was to evaluate this radiopharmaceutical in the assessment of ventilation, with particular emphasis on its use in the differential diagnosis of PE.

Materials and methods

Patients

63 patients were studied, 58 of whom had been referred because of suspected PE.

There were 27 males and 36 females with an age range 22–78 years. 31 consecutive patients referred for routine ventilation ($^{81}\text{Kr}^{\text{m}}$) and perfusion ($^{99}\text{Tc}^{\text{m}}$ -MAA) scans underwent an additional ventilation study using Technegas. A further 23 patients had a Technegas ventilation study followed by perfusion imaging on days when $^{81}\text{Kr}^{\text{m}}$ gas was not available. In the final phase of the study, nine patients had an initial perfusion study with a lower than normal dose of $^{99}\text{Tc}^{\text{m}}$ -MAA followed by a Technegas ventilation study.

Equipment and procedure

The Technegas generator is a mobile, microprocessor controlled device which consists of a shielded 7 litre chamber above two electrodes between which a graphite crucible can be inserted. Access to the electrodes is via a drawer in the front of the generator. Technegas is produced by loading 250–400 MBq of $^{99}\text{Tc}^{\text{m}}$ -pertechnetate in 0.1 ml saline into the crucible, evaporating this to dryness and then heating to 2500°C in an atmosphere of high purity argon. The physical process of Technegas production has not been described in the literature. A possible mechanism is that a sodium pertechnetate aerosol is initially produced by condensation of sodium pertechnetate vapour. Technegas is then formed by condensation of carbon vapour onto the sodium pertechnetate particles which act as nucleation centres. Once generated, the Technegas can be used for up to 10 min, after which the patient outlet port automatically shuts.

To inhale Technegas the patient was seated as for a posterior lung view in front of the gamma camera (either an IGE 400A/T maxicamera or an Elscint Dymax LF, each fitted with a low energy general purpose collimator). For administration a plastic tube is connected to the generator outlet port. The other end is connected to a delivery set consisting of a mouthpiece, a filter and two one-way valves. The operator can control whether the generator outlet port is connected to the Technegas chamber or to room air. Care was taken to ensure that the patient was relaxed and had ample time to practice the inhalation technique, which involved taking a slow deep inspiration and breath-holding for 5 s before expiring and returning to normal tidal breathing.

Initially the patient breathed room air and was then switched to Technegas at the start of the slow deep inspiration. On expiration any Technegas not deposited in the lungs was trapped on the filter and the patient returned to tidal breathing of room air. The count rate was monitored by the gamma camera and the procedure repeated until the desired rate of 1600 counts/s was reached, corresponding to a total deposited activity of approximately 20 MBq. Following administration the disposable delivery set and generator were removed. With the patient remaining seated, 200 kcount images were then obtained in posterior, anterior, right posterior oblique and left posterior oblique projections. Each image took 2–3 min to acquire. Computer images on a 64×64 matrix were acquired simultaneously with analogue images.

On completion of the Technegas image acquisition and with the patient remaining seated, an intravenous injection of 100 MBq $^{99}\text{Tc}^{\text{m}}$ -MAA was given, thus achieving a ratio of $^{99}\text{Tc}^{\text{m}}$ -MAA:Technegas of 5:1. Four images (400 kcounts) were acquired in the projections listed above, each taking approximately 30 s. Care was taken to ensure that patient positioning was the same for both studies.

54 patients had ventilation and perfusion studies performed in this way. 31 of these patients then went on to have a second ventilation study with $^{81}\text{Kr}^{\text{m}}$ gas obtained by passing air through an $^{81}\text{Rb}/^{81}\text{Kr}^{\text{m}}$ generator (Clark et al, 1978). The patient remained seated in front of the gamma camera (with a low energy general purpose collimator fitted) and performed tidal breathing through a ventilated face mask usually for less than 1 min to acquire 400 kcount images as before.

In the group of nine patients who had a Technegas ventilation study following rather than preceding the perfusion study, an intravenous injection of 10–20 MBq $^{99}\text{Tc}^{\text{m}}$ -MAA was given, and 200 kcount images (2–5 min) were then obtained in the four projections previously described. Technegas was administered to achieve a posterior count rate of 4000 counts/s (equivalent to 50 MBq Technegas and a target $^{99}\text{Tc}^{\text{m}}$ -MAA:Technegas ratio of 1:5), and 200 kcount images (less than 1 min) were obtained as before with special care taken to ensure accurate positioning of the patient.

Results

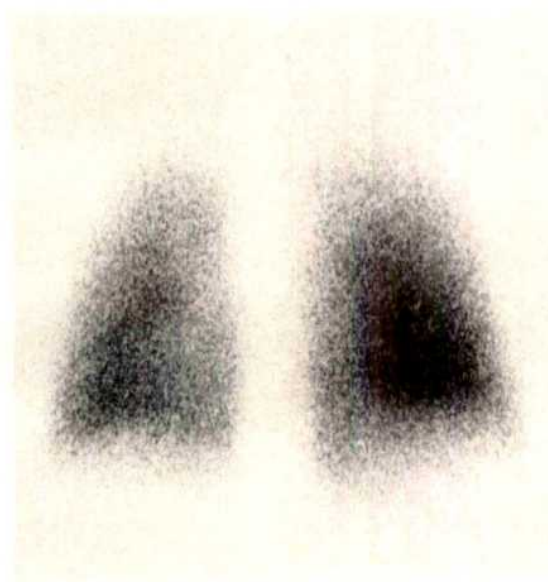
Table I shows the overall scan result in each of the groups studied.

Each scan was assessed by two independent, experienced observers: it was reported as normal (Fig. 1) or as consistent with PE if one or more perfusion defects were seen in either lung, which were not matched by a corresponding decrease in ventilation (Fig. 2). An abnormal scan not typical of PE (Abnormal-no PE) was reported when a matching decrease in ventilation and perfusion was seen or when a reverse mismatch was noted (a ventilatory defect larger than the perfusion defect).

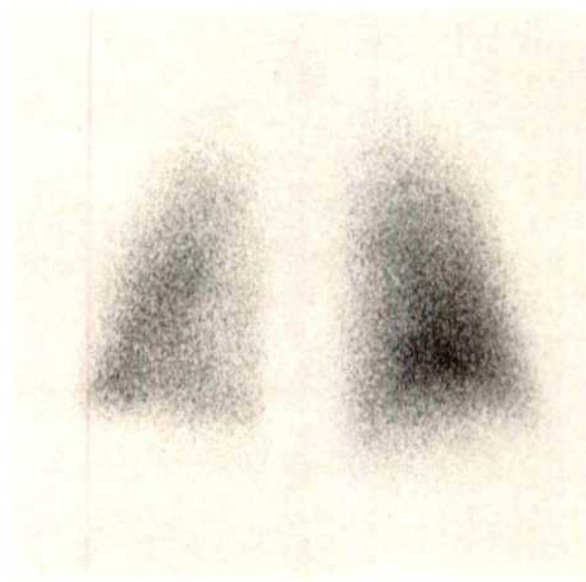
Within Group 1 the $^{81}\text{Kr}^{\text{m}}$ and Technegas images were found to be comparable and of the same diagnostic

Table 1. Overall scan results

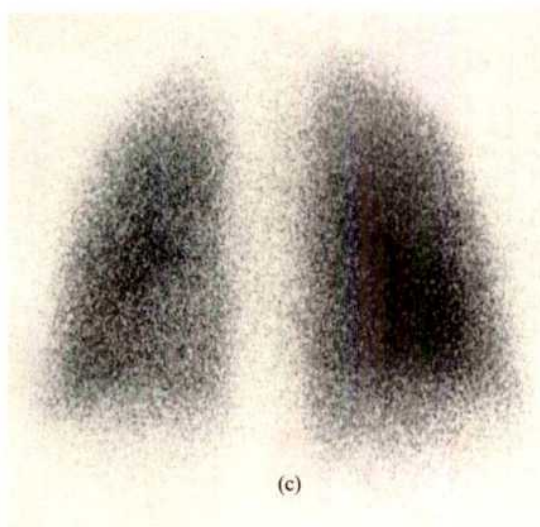
Scan report	Group 1: Technegas + ⁹⁹ Tc ^m -MAA + ⁸¹ Kr ^m	Group 2: Technegas + ⁹⁹ Tc ^m -MAA	Group 3: ⁹⁹ Tc ^m -MAA (low dose) + Technegas	Total
PE	7 (23%)	8 (35%)	5 (56%)	20 (32%)
Normal	13 (42%)	6 (26%)	2 (22%)	21 (32%)
Abnormal—no PE	11 (35%)	9 (39%)	2 (22%)	22 (34%)
Total	31	23	9	63



(a)



(b)



(c)

Figure 1. Posterior view of normal lungs. (a) Perfusion—⁹⁹Tc^m-MAA; (b) ventilation—Technegas; (c) ventilation—⁸¹Kr^m gas.

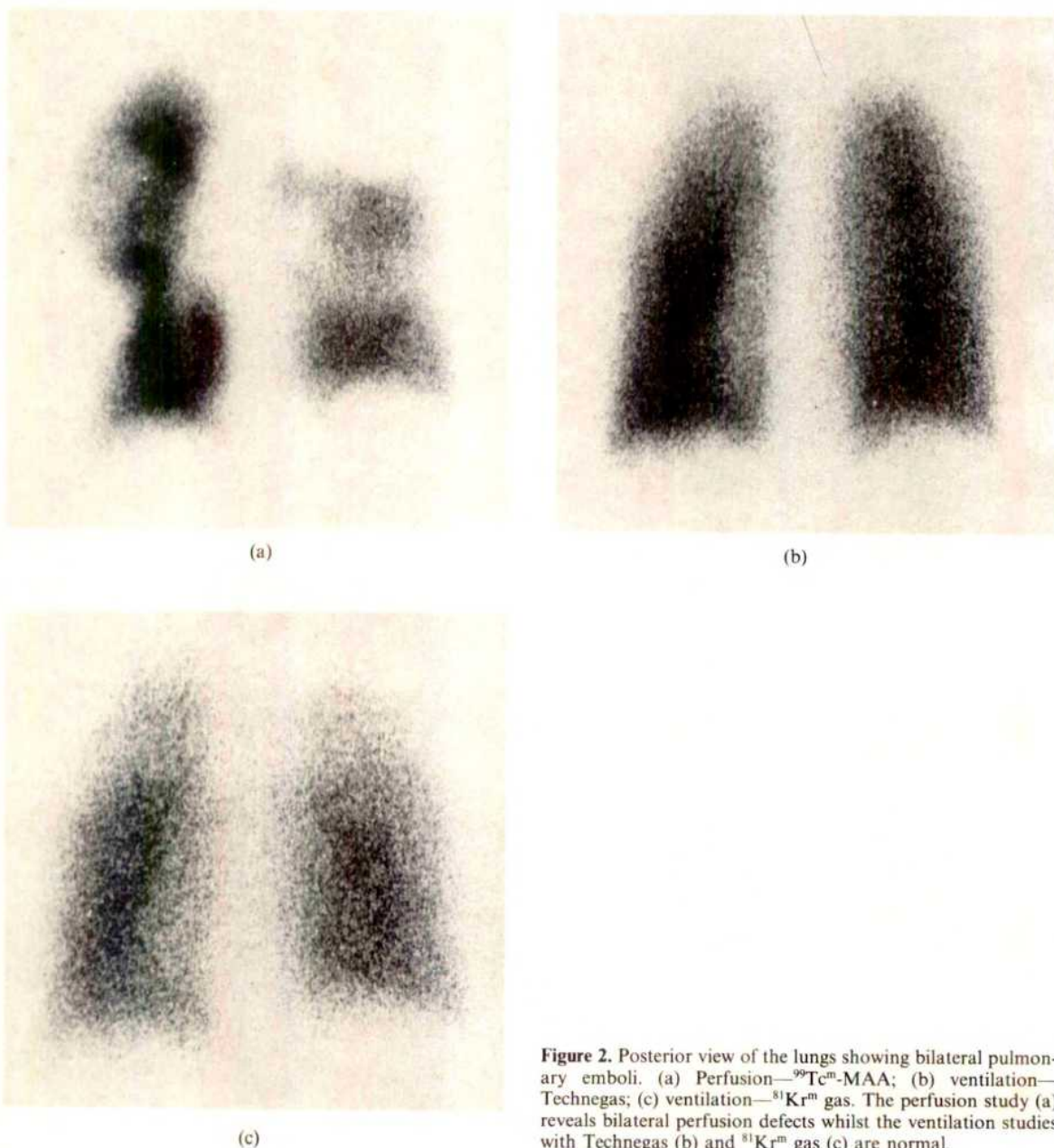


Figure 2. Posterior view of the lungs showing bilateral pulmonary emboli. (a) Perfusion— ^{99m}Tc -MAA; (b) ventilation—Technegas; (c) ventilation— ^{81}Kr gas. The perfusion study (a) reveals bilateral perfusion defects whilst the ventilation studies with Technegas (b) and ^{81}Kr gas (c) are normal.

quality in 30 patients. In only one case did the two ventilatory agents lead to differing diagnoses. In this patient, a single perfusion defect on the lateral aspect of the right lung was found to be normally ventilated with Technegas and to have a matching defect with ^{81}Kr (Fig. 3). A pulmonary embolus would therefore have been reported from the Technegas study but not from the krypton study. In seven patients the distribution of Technegas, although comparable with that of ^{81}Kr , was felt to mimic the perfusion pattern more closely. In

five patients there was greater deposition of Technegas at the lung bases relative to the apices, which was not seen on the ^{81}Kr study (Fig. 4).

Within the group as a whole, "hot spots" (regions of high count density) were noted on the Technegas study in a total of nine patients (14%) (Fig. 5) and extrapulmonary deposition (EXPD—Technegas deposition in the oropharynx, neck, thyroid, trachea or stomach) in 19 (30%) (Fig. 6). The two were associated in four patients (6%). Pulmonary pathology other than the

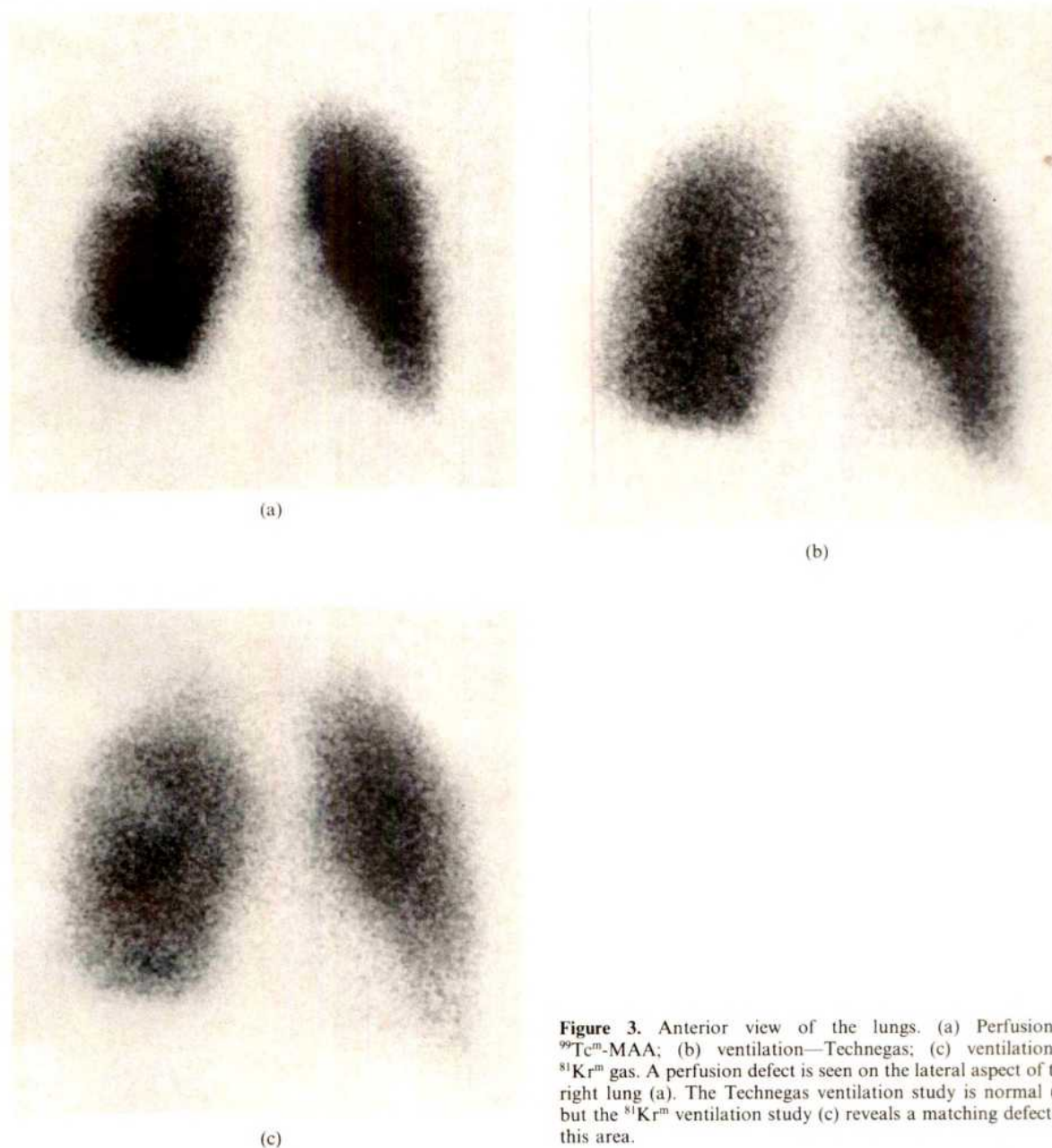


Figure 3. Anterior view of the lungs. (a) Perfusion—⁹⁹Tc^m-MAA; (b) ventilation—Technegas; (c) ventilation—⁸¹Kr^m gas. A perfusion defect is seen on the lateral aspect of the right lung (a). The Technegas ventilation study is normal (b) but the ⁸¹Kr^m ventilation study (c) reveals a matching defect in this area.

suspected thromboembolic disease was known to be present in 17 patients (27%), and of these three (18%) had hot spots and seven (41%) had EXPD.

Images of diagnostic quality were obtained for both ventilation and perfusion in the Group 3 patients (Fig. 7). In four cases the perfusion image could be compared with previously performed perfusion studies using "normal" dosage of ⁹⁹Tc^m-MAA. The diagnostic value of the low dose perfusion image was not significantly altered.

Discussion

In modern clinical practice it is essential to diagnose PE by an objective method before treatment is instituted. This could be provided by ventilation-perfusion scintigraphy if a ventilation radiopharmaceutical were readily available and easily administered.

Technegas provides images of quality comparable with those obtained using other agents. Advantages include the optimum physical properties of ⁹⁹Tc^m and continuous availability. Furthermore, in contrast to the

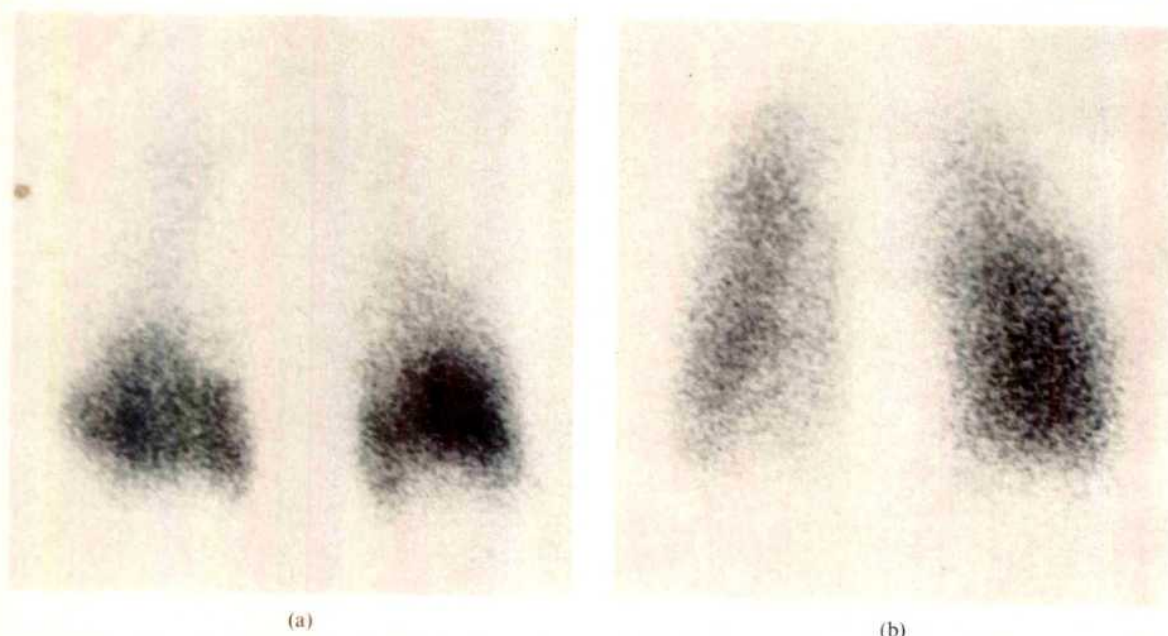


Figure 4. Posterior view of the lungs. (a) Ventilation—Technegas; (b) ventilation— $^{81}\text{Kr}^m$ gas. A marked difference is seen in the pattern of deposition of Technegas (a) when compared with $^{81}\text{Kr}^m$ gas (b). There is pronounced basal deposition of Technegas.

cumbersome apparatus required by some aerosol delivery systems, the Technegas generator is safe, lead shielded and compact. Further studies to assess the effects of variable rates and depths of inhalation on Technegas deposition are needed, but from this series it

would appear that the size of the particles is sufficiently small for them to reach the alveoli and that deposition is less dependent on inhalation technique than with other radiolabelled aerosols. As Technegas is not significantly cleared from the lungs, multiple views and indeed tomo-

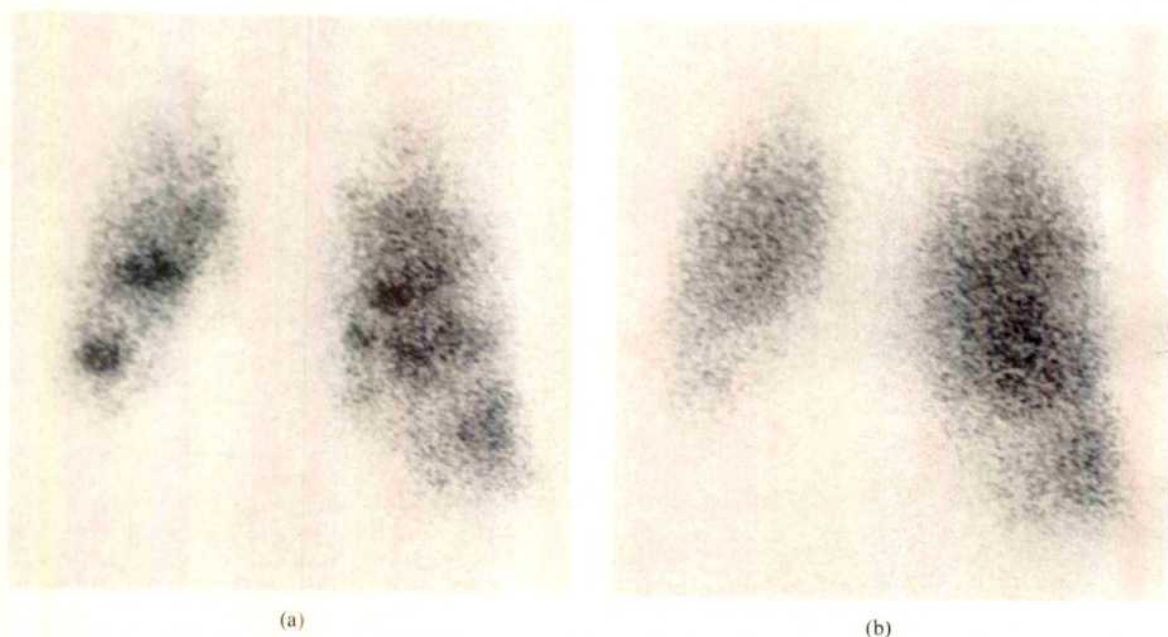


Figure 5. Posterior view of the lungs. (a) Ventilation—Technegas; (b) ventilation— $^{81}\text{Kr}^m$ gas. Both ventilation studies show a left sided basal defect. In addition a number of hot spots are seen on the Technegas image (a) whereas $^{81}\text{Kr}^m$ distribution is more uniform (b).

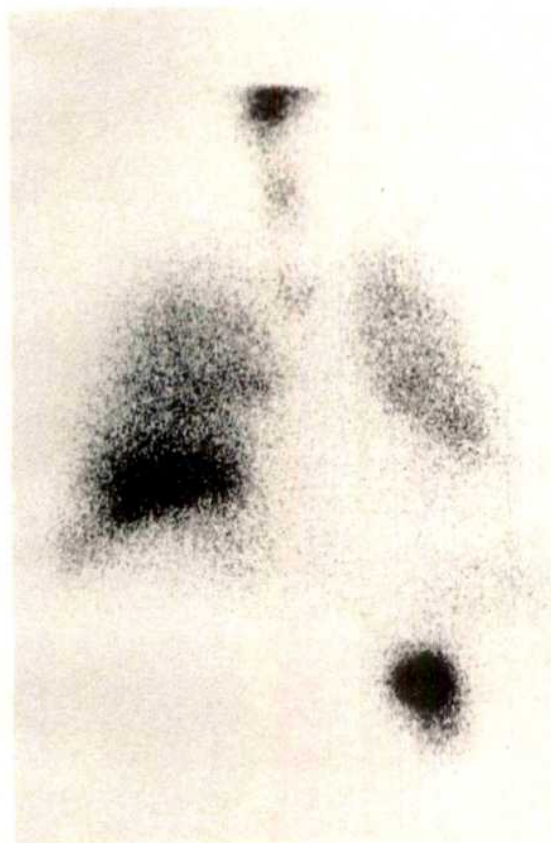


Figure 6. Anterior view of the lungs showing EXPD of Technegas in the oropharynx, neck, trachea and stomach.

graphic imaging are possible following a single administration (Burch et al, 1986).

Our results are similar to those obtained by Peltier et al (1990) in a comparison of Technegas with ⁸¹Kr^m. However, there was some difference between the studies in the base to apex gradient of the Technegas distribution and this is discussed later.

The majority of patients studied experienced no major problems with the inhalation technique. However, it is possible for patients to both inhale and exhale around as well as through the mouthpiece, thus reducing the concentration of Technegas inhaled and possibly contaminating the gamma camera room. Other patients may experience difficulty with deep breathing or breath-holding. Such difficulties have been noted by other authors (DeGeeter et al, 1990), and some would suggest that for this reason Technegas is unsuitable for use in very ill patients and difficult to use in patients with known severe pulmonary disease. Our experience is that the great majority can cooperate with the inhalation technique and that it is essential to teach with care the breathing pattern required with a number of practice runs to identify possible problems for the particular patient. Some patients, particularly those with severe

chronic airflow obstruction, need to remove the mouthpiece between breaths in order to inhale room air. This is acceptable, and if the patient is aware that this is permissible he is usually able to cooperate fully.

It is interesting to note that there was only one disagreement in diagnosis out of the 31 cases who were investigated using both ⁸¹Kr^m and Technegas for ventilation imaging. The patient was a young previously healthy female in whom the clinical suspicion of PE was low and the chest X-ray normal. A single, small perfusion defect was seen on the upper lateral aspect of the right lung on both the anterior and the posterior views. The lungs were normally ventilated on the Technegas study, but a corresponding area of decreased ventilation was seen on the krypton study. No explanation can be offered for this discrepancy at the present time. In no other case in this series has such a clear discrepancy between the two radiopharmaceuticals been seen.

The presence of hot spots has been well documented on aerosol ventilation images (Arnot et al, 1986), and in patients with chronic obstructive airways disease several studies have noted increased central/large airway deposition with relatively less peripheral penetration and overall patchy images. Hot spots are thought by some authors to indicate areas of local turbulence and therefore to be a reflection of the severity of airways obstruction. In this series, 'hot spots' were seen in 14% of the total patient group and in 18% of those with known pulmonary disease. EXPD was seen in 30% of the total group and in 41% of those with known pulmonary disease. Hot spots and EXPD were themselves related in only 6% of the total patient group. This study failed to demonstrate a consistent relationship between a clinical diagnosis of airways obstruction and the presence of hot spots. We did not, however, have any definitive measure of lung function. To clarify this, further studies are planned to compare patterns of Technegas deposition in known chronic lung disease with indices of pulmonary function.

The presence of EXPD and, in particular, its significance in patients with known pulmonary disease merit further examination. EXPD may arise as a result of technical failure within the Technegas generator. For example, a sodium pertechnetate aerosol could be produced if the burn temperature were lower than usual. Free pertechnetate within the aerosol will be absorbed and trapped by the thyroid gland. Both free pertechnetate and Technegas within the oropharynx can be swallowed and thus appear within the oesophagus or stomach. Alternatively, the patient may experience difficulty with the inhalation technique or breath-holding, resulting in Technegas deposition within the oropharynx or supralaryngeal area. Within the patient group as a whole, on average six breaths were needed to achieve the desired count rate. If the patients with both hot spots and EXPD are excluded the average number of breaths required was four. Patients with hot spots needed an average of 10 breaths and those with EXPD needed 11. The association between EXPD and known pulmonary disease may, therefore, merely reflect the fact that these

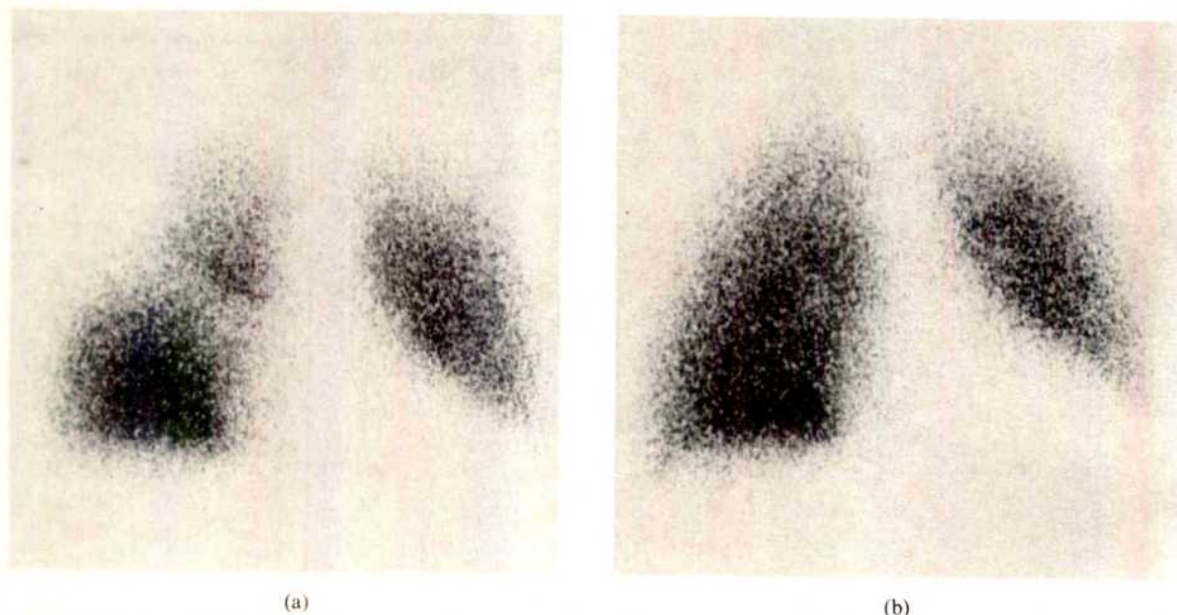


Figure 7. Anterior view of lungs showing right pulmonary embolus. (a) Perfusion— $^{99}\text{Tc-m-MAA}$; (b) ventilation—Technegas. This patient had a low dose perfusion study followed by Technegas ventilation.

patients experience more difficulty with the inhalation technique.

In five patients we found that the increase in count density from apex to base was greater for Technegas than for $^{81}\text{Kr}^m$. This may reflect a genuinely high basal ventilation in these patients which, owing to the fact that $^{81}\text{Kr}^m$ underestimates ventilation at high rates (Jones, 1978), was better seen with Technegas. Alternatively, this could have been due to a difference in inhalation pattern for these patients, although efforts were made to ensure that the same administration technique was used for all. Agnew et al (1984) compared the distribution of $5\text{ }\mu\text{m}$ $^{99}\text{Tc}^m$ particles and $^{81}\text{Kr}^m$ in normals and asthmatic subjects and found an increase in the base to apex ratio of the aerosol distribution compared with that of $^{81}\text{Kr}^m$ in the latter group. It was suggested that this was due to the closure of basal airways in asthmatics in early inspiration when the $^{81}\text{Kr}^m$ concentration is highest. Later, when the basal airways open, the $^{81}\text{Kr}^m$ concentration has fallen whereas the aerosol concentration is constant throughout. In our study we may have observed a similar effect and we are currently studying this in a group of patients with various respiratory diseases in whom indices of lung function have been measured. Peltier et al (1990) did not find any significant difference in the apex to base distribution of Technegas compared with that of $^{81}\text{Kr}^m$. This may have been because the patients inhaled Technegas in a semirecumbent or supine position. In these positions there may be changes in ventilation because of gravity from anterior to posterior rather than from apex to base.

The final phase of the study comprised the perform-

ance of Technegas ventilation studies following low dose perfusion studies, *i.e.* a reversal of the usual procedure. In all nine patients undergoing this protocol, diagnostic images were obtained for both studies. If adopted on a wider scale this protocol would permit avoidance of an unnecessary ventilation study when the perfusion study is normal. The perfusion images, despite decreasing the number of counts obtained from the usual 400k to 200k, do take longer to acquire with consequent increased risk of patient movement and inaccuracies. It would be possible to decrease imaging time by a further decrease in the number of counts obtained but this would impair image quality. An increase in the dose of $^{99}\text{Tc-m-MAA}$ followed by computer subtraction of all perfusion images from the ventilation images would also decrease imaging time. This would require accurate alignment of the images, and placement of markers would probably be necessary to ensure this. Image quality may be decreased and there would be an increase in both the time and complexity of the acquisition and the processing procedures. Furthermore, the subjective interpretation of the subtracted images may contribute errors. Thus, although such protocols appear to offer some advantages over the more usual procedures, they still require further evaluation in a larger group of patients.

Conclusion

Technegas is easy to prepare and administer. Good quality ventilation images are produced which are comparable in most instances with those obtained with $^{81}\text{Kr}^m$ gas although imaging times are longer.

Administration appears feasible even in patients with compromised respiratory function. Unlike ⁸¹Kr^m, Technegas can be made readily available, thus improving the diagnostic service for suspected PE.

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Organ doses received by atomic bomb survivors during radiological examinations at the Radiation Effects Research Foundation

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Abstract. When evaluating the risks of oncogenesis and cancer mortality following exposure to the radiations of the atomic bombs (A-bombs), the medical X-ray doses received by the A-bomb survivors must also be estimated and considered. Using a human phantom, dosimetry was performed to estimate the X-ray doses received by A-bomb survivors during medical examinations at the Radiation Effects Research Foundation (RERF) as part of the long-term follow-up on the Adult Health Study (AHS). These examinations have been estimated to represent nearly 45% of the survivors' cumulative medical irradiation dose. Doses to the salivary glands, thyroid gland, lung, breast, stomach and colon were measured using thermoluminescent dosimeters. The results, which are reported here, will aid in estimating organ doses received by individual AHS participants.

This investigation was prompted by observations of excess mortality among atomic bomb (A-bomb) survivors due to leukaemia and cancers of the lung, breast, stomach and colon (Shimizu et al, 1990), and from radiation-induced tumours of the thyroid gland and salivary glands (Belsky et al, 1975; Takeichi et al, 1976; Prentice et al, 1982). When estimating the risk of oncogenesis and cancer mortality as a result of A-bomb radiation exposure, medical X-ray doses received by the survivors must also be estimated and carefully considered.

During routine biennial visits to the Radiation Effects Research Foundation (RERF), each lasting 1 day, the participants in the Adult Health Study (AHS) have received regular radiological examinations, in addition to those received at other institutions. During a 2-week survey, it was shown (Sawada et al, 1979) that 47% of the total X-ray examinations received by AHS participants were those conducted at RERF in Hiroshima, whereas the corresponding rate in Nagasaki was 46%. Thus, estimates of doses received at RERF are necessary in order to estimate the subjects' current total medical X-ray doses.

In the present study, typical RERF radiological examinations were reproduced using a human phantom and thermoluminescent dosimeters (TLD) positioned at the site of the salivary glands, thyroid gland, lung,

breast, stomach and colon. These dose measurements will supplement the cumulative active bone marrow, gonad and surface doses per examination that were documented earlier (Antoku et al, 1986) in AHS subjects.

Doses were estimated by the type of examination and by irradiated organ, using TLDs. The sensitivity of each TLD was carefully determined, by dose, tube voltage and exposure direction (Kato et al, 1989) using an Exadin A2 Shonka-Wyckoff chamber (Warrenville, IL, USA).

Experimental equipment

The following equipment was used in this study.

Human phantom: an Alderson Rando adult (female) human phantom (Alderson Research Laboratories, Stamford, USA), which approximated to an average Japanese adult male and female.

Thermoluminescent detectors: Kasei Optonix MSO-S TLD $Mg_2SiO_4(Tb)$, cylindrical chips (Kasei Optonix, Odawara, Japan).

Thermoluminescent readout system: Harshaw Model 2000A Thermoluminescent Measurement Apparatus and Model 2000B Automatically Integrating Picoammeter (Harshaw/Nuclear Systems, Cleveland, OH, USA).

X-ray apparatus: Toshiba X-ray apparatus with full-wave rectification of single-phase alternating current, which was inverted to high-frequency current (Model DRX2603HD X-ray tube, Model DC-15K controller

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and Model DG-15F transformer) (Toshiba Medical Systems, Tokyo, Japan), and Hitachi fluoroscopy apparatus with full-wave rectification of three-phase alternating current (Model DR-125-22 TV) (Hitachi Medical Corporation, Tokyo, Japan).

Dosimetry methodology

Thermoluminescent detectors (TLDs) were annealed in an electric furnace at 400°C for 7 hours and subsequently were inserted at various sites in the human phantom, as shown in Table I and Fig. 1. One dose-meter was used at each measurement site. After exposing the phantom to X rays, the TLDs were removed, stored in the dark for a minimum of 90 minutes, and then were assessed for thermoluminescence. The X-ray exposures and TLD measurements were repeated two to four times for each radiological examination to minimize experimental errors. Details of these TLD measurements have been reported separately (Kato et al, 1989).

Table I. Dose measurement sites in the human phantom

No.	Section number ^a	Measurement site ^b
1	6	Right parotid
2	6	Left parotid
3	8	Right submandibular gland
4	8	Left submandibular gland
5	8	Sublingual gland
6	9	Right thyroid gland
7	9	Left thyroid gland
8	17	Right breast (1)
9	17	Right breast (2)
10	17	Left breast (3)
11	17	Left breast (4)
12	13	Right lung (1)
13	13	Left lung (2)
14	15	Right lung (1)
15	15	Left lung (2)
16	18	Right lung (1)
17	18	Right lung (2)
18	18	Right lung (3)
19	18	Left lung (4)
20	18	Left lung (5)
21	18	Left lung (6)
22	20	Right lung (1)
23	20	Left lung (2)
24	23	Stomach
25	26	Large intestine (1)
26	26	Large intestine (2)
27	31	Large intestine
28	32	Right ovary
29	32	Left ovary
30	—	Surface (centre of irradiation field)

^aThe human phantom consists of successive 2.5 cm thick transverse sections. The sections were numbered beginning at the vertex.

^bMeasured sites belonging to a section and the same organ were numbered in order from right to left, as indicated in parentheses.

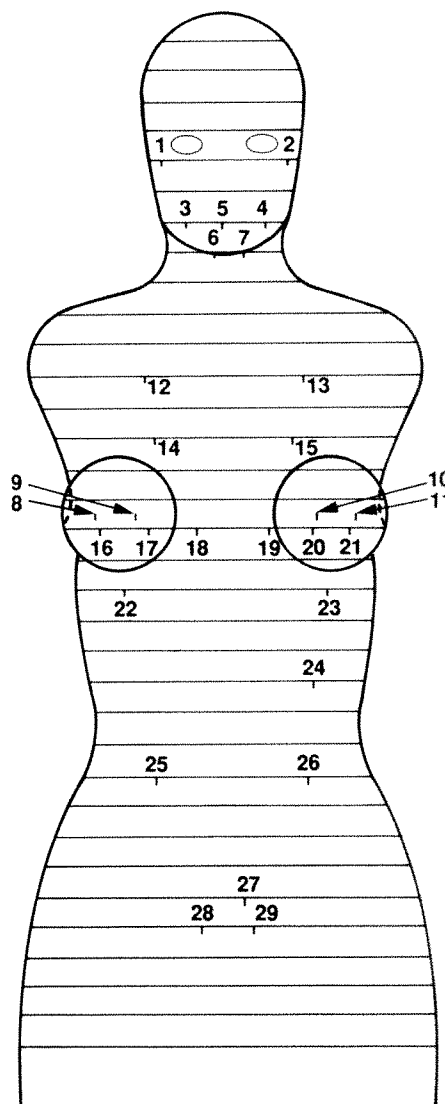


Figure 1. Diagram showing the dose measurement sites in the Alderson Rando human adult phantom. Numbers indicate the measurement sites (see Table I).

X-ray exposures were made using the radiological techniques employed at the Atomic Bomb Casualty Commission (ABCC)/RERF; Table II shows some representative technical factors used at RERF in Hiroshima. Doses for neck and rib examinations were measured using a 100 cm focus-film distance (FFD). Adjustments for differences in FFD were made by applying the "inverse square" law relationship. The measured thermoluminescence values were converted to exposures using the individual sensitivity calibration data of the detectors (Kato et al, 1989). The factor for converting exposures to absorbed doses was 34 (Gy kg/C), which is equivalent to the conversion factor for 30–50 keV photons in muscle (ICRU, 1979). The tube

voltage was restricted to the range 50–120 kVp. The above conversion factor was assumed to be independent of tube voltage and measurement site, allowing for 7% uncertainty. Furthermore, except for the stomach, the volume of each organ was divided so that each resulting part contained one measured site. The average dose to each organ was calculated by obtaining the mean, weighted by the volume, of each part. The doses obtained were corrected to those X-ray sets which actually delivered them during examinations using the ratios of the outputs of the different X-ray apparatus. Doses to the active bone marrow were not measured in the present study.

Results

Some of the organ doses estimated using the above methods are shown in Tables III and IV. The X-ray equipment and technical factors used at ABCC/RERF in Nagasaki were the same as those at ABCC/RERF in Hiroshima. The machines at ABCC/RERF in Nagasaki were replaced in 1980, and the outputs of these machines and the qualities of the X rays were carefully investigated. The estimated organ doses from examinations now conducted at RERF in Nagasaki are shown in Table IV. Doses per milliamperere-second during neck

radiography are shown as examples in Table V. The doses within the irradiation fields were reproducible to within 3% of the average value. Doses to the stomach and colon, located far from the neck regions, varied by more than 3%; however, the doses to these organs were very low. Only one measured site was used for the stomach dose. Moreover, the position was changed slightly, and adjustments were made by using depth profiles of X-ray dose in a human phantom (Antoku et al, 1972). The uncertainties in stomach doses were estimated to be 23%. The uncertainties shown in Table V include: (i) that of the conversion factor from exposure to radiation absorbed doses (7%); (ii) that of the calibration factor for the standard ionization chamber (Exradin A2 Shonka-Wyckoff Chamber, Warrenville, IL, USA) (Kato et al, 1989) (3.7%); (iii) the reproducibility of the conversion factor from TL-intensity to exposure (4–6%); and (iv) the reproducibility of the TL-measurements in the phantom experiment.

The surface doses are important because they indicate both the maximum dose and the X-ray output. However, they are higher than the free-in-air dose at the same measurement site, because of the addition of backscattered X rays. Table VI shows doses measured by placing the ionization chamber mentioned above in

Table II. Technical factors for radiography and fluoroscopy (upper gastrointestinal series) at RERF, Hiroshima

Examination site	Projection	Current × exposure time (mAs)	Tube voltage (kVp)	Added filtration (mm Al)	FFD (cm)	Film size (inches)
Skull	PA	25	84	3.0	91	10 × 10
	Lateral	25	74	3.0	91	10 × 10
	AP	25	84	3.0	91	10 × 10
Sinuses	PA	20	78	3.0	91	8 × 10
	Lateral	20	66	3.0	91	8 × 10
Mastoid	PA-oblique	20	82	3.0	91	8 × 10
C-spine	AP	20	90	3.0	102	8 × 10
	Lateral	28	78	3.0	183	8 × 10
	AP-oblique	28	78	3.0	183	8 × 10
Neck	AP	10	90	3.0	183	8 × 10
	Lateral	10	90	3.0	183	8 × 10
T-spine	AP	20	100	3.0	102	11 × 14
	Lateral	30	110	3.0	102	11 × 14
L-spine	AP	20	100	3.0	102	14 × 17
	Lateral	40	120	3.0	102	14 × 17
	AP-oblique	40	100	3.0	102	14 × 17
Chest	PA	3	120	3.0	183	14 × 17
	Lateral	6	120	3.0	183	14 × 17
	PA-oblique	3	115	3.0	183	14 × 17
Rib	PA	12	80	3.0	183	10 × 12
	PA-oblique	16	98	3.0	91	10 × 12
Abdomen	AP	20	100	3.0	102	14 × 17
Pelvis	AP	20	100	3.0	102	14 × 17
Gallbladder	PA	30	100	3.0	102	14 × 17
	PA-oblique	30	100	3.0	102	14 × 17
Chest	Tomo, AP	40	80	2.5	102	8 × 10
Upper GI (Flx)	—	0.5 mA	90	3.0	—	—
Upper GI (Spot)	—	PHT	90	3.0	—	—

FFD: focus–film distance; Flx: fluoroscopy; Tomo: tomography; PHT: phototimer.

the centre of the exposure field with and without a Mix-D block phantom behind it. The configuration of the surface of the human body differs by examination site, and variations in doses due to scattering were observed accordingly.

The X-ray output of the apparatus used in the experimental study and an example of measurement of the attenuation by aluminium filters are shown in Fig. 2. At RERF, the outputs and qualities of the X-rays were periodically checked and recorded. The half-value layers for 100 kVp X rays for the three X-ray sets were 4.4, 4.0 and 4.1 mm Al, respectively. The variations in several organ doses during chest radiography, due to the aluminium filtration, are shown in Fig. 3. Tables III and IV show doses that were adjusted only for differences in output for each of the X-ray sets recently in use and for the experimental apparatus. The uncertainties due to the differences in beam qualities were 6%. Table V shows doses without adjustments for the differences in output. Dosimetry for the upper gastrointestinal (GI) series was performed during simulations of the actual examinations, each including 16 spot radiographs. The dose-rates shown in Table III were calculated from the results of dosimetry and the output rates of fluoroscopy and

spot radiography, based on the assumption that the dose distribution from fluoroscopy was the same as that from spot radiography. Exposures that were incurred in the past can be estimated from the ABCC/RERF records of examinations and the technical factors that were used, the X-ray output at the times of exposures, and from the doses measured in the present study.

The radiation-absorbed doses indicated in Tables III and IV include the uncertainties in doses at each measurement site (Table V), the calculations of mean values in each organ, and the adjustments for the difference in output and beam quality mentioned above. As shown in Table I, each organ was divided into sufficiently small portions so that each portion would include one TLD, except in the case of the stomach. According to the depth profiles of the radiation absorbed dose reported by Antoku et al (1972), the uncertainties in the calculations of the mean values in each organ are estimated to be less than 10%. The X-ray equipment used in the present experiment is routinely used for tomography. The total uncertainties of the doses from tomography were 26–33%; for the other radiography, 32–39%.

The doses obtained experimentally were adjusted

Table III. Doses from radiography and fluoroscopy at RERF, Hiroshima (unit: 10^{-2} mGy/exposure)

Examination site	Projection	Surface	Salivary	Thyroid	Breast	Lung	Stomach	Colon
Skull	PA	176	46	25	0.36	1.0	0.11	0.08
	Lateral	125	64	64	0.65	0.64	0.011	0.053
	AP	183	67	117	1.4	1.2	0.091	0.11
Sinuses	PA	103	26	8.7	0.16	0.39	0.34	0.038
	Lateral	74	39	24	0.32	0.18	0.19	0.024
Mastoid	PA-oblique	115	11	5.9	0.14	0.52	0.058	0.049
	AP	194	89	171	3.1	22	0.25	0.13
C-spine	Lateral	59	27	32	0.31	1.9	0.020	0.020
	AP-oblique	68	35	50	0.67	4.3	0.040	0.028
Neck	AP	28	11	23	0.26	2.4	0.11	0.0070
	Lateral	33	16	17	0.57	0.69	0.0036	0.0049
T-spine	AP	316	9.1	17	203	71	63	8.7
	Lateral	800	5.8	7.5	25	185	5.5	1.2
L-spine	AP	300	0.99	1.3	5.4	5.3	171	135
	Lateral	1492	2.1	0.98	12	21	80	200
	AP-oblique	659	2.1	2.7	14	16	135	200
Chest	PA	14	0.94	1.2	2.0	6.6	2.3	0.25
	Lateral	33	6.1	8.0	11	12	2.1	0.35
	PA-oblique	11	0.48	1.8	0.85	5.0	2.2	0.17
Rib	PA	74	0.63	0.78	4.6	19	0.89	0.18
	PA-oblique	159	1.7	2.2	5.6	66	4.5	0.18
Abdomen	AP	294	0.88	1.3	5.5	5.6	80	96
Pelvis	AP	326	0.33	0.54	1.6	0.19	46	84
Gallbladder	PA	492	0.73	0.46	4.2	15	105	157
	PA-oblique	522	0.37	0.24	2.1	12	183	88
	(Erect)	456	0.24	0.14	1.2	4.2	139	74
Chest (Tomo)	AP	127	0.95	1.2	53	13	13	0.22
Upper GI (Flx) ^a		328 ^b	0.83	1.2	34	18	234	77
Upper GI (Spot)		101 ^b	0.25	0.36	11	5.6	72	24

Tomo: Tomography, Flx: Fluoroscopy, Spot: Spot radiography.

^aUnit: 10^{-2} mGy/min; ^bbased on Antoku and Russell (1971).

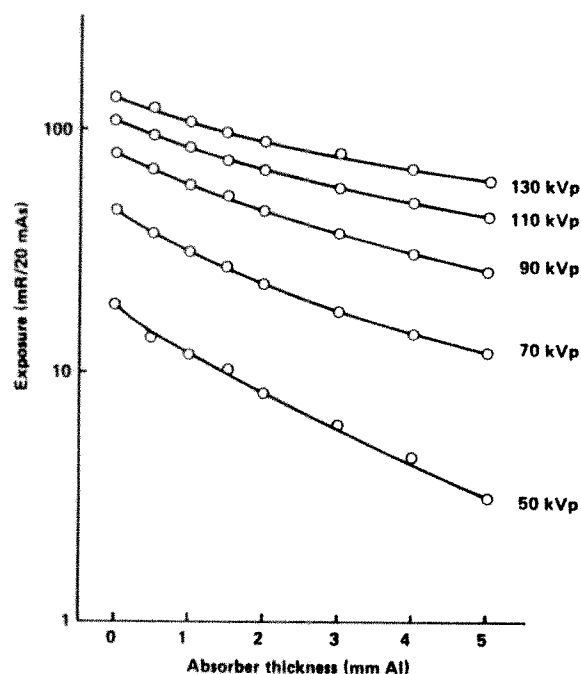


Figure 2. Output of X-ray apparatus used for experimental study, September 1987. Each exposure per 20 mAs was measured using the following technical factors: a 100 cm focus-ionization chamber distance, a 20 cm $\times$ 20 cm beam size, and a 0.5 mm Al inherent filtration (excluding added filter).

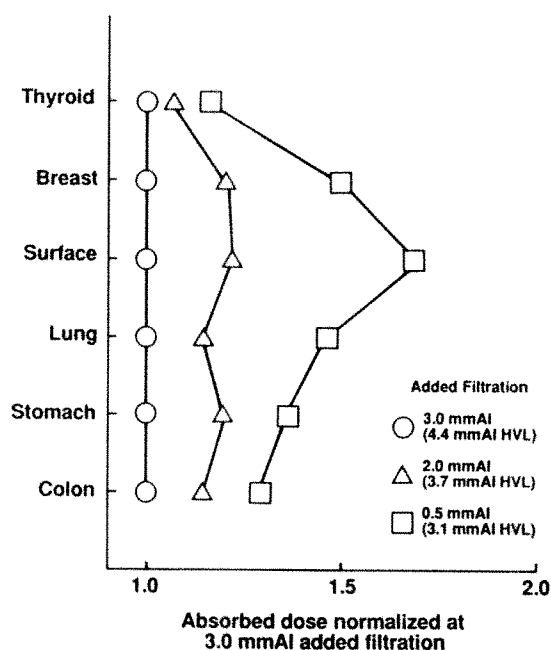


Figure 3. Organ doses from chest radiography (posterior-anterior projection; 100 kVp tube voltage). Doses were normalized at 3.0 mm Al added filtration. The half-value layers for the X rays were 4.4 mm Al at 3.0 mm Al added filtration, 3.7 mm Al at 2.0 mm Al added filtration and 3.1 mm Al at 0.5 mm Al added filtration.

Table IV. Radiography doses at RERF, Nagasaki (unit: 10^{-2} mGy/exposure)

Examination site	Projection	Surface	Salivary	Thyroid	Breast	Lung	Stomach	Colon
Skull	PA	132	34	19	0.27	0.79	0.079	0.062
	Lateral	96	49	49	0.50	0.49	0.0086	0.041
	AP	137	50	87	1.0	0.93	0.068	0.082
Sinuses	PA	49	13	4.1	0.74	0.18	0.16	0.018
	Lateral	38	20	12	0.16	0.092	0.096	0.012
Mastoid	PA-oblique	91	8.6	4.7	0.11	0.41	0.046	0.039
C-spine	AP	78	35	68	1.3	8.9	0.10	0.051
	Lateral	28	13	15	0.15	0.92	0.0097	0.0093
	AP-oblique	32	17	24	0.32	2.0	0.019	0.013
Neck	AP	8.6	3.4	7.1	0.081	0.78	0.034	0.0022
	Lateral	10	5.0	5.4	0.18	0.22	0.0011	0.0015
T-spine	AP	218	6.3	11	140	49	44	6.0
	Lateral	368	2.7	3.4	10	85	2.5	0.55
L-spine	AP	360	1.19	1.6	6.4	6.2	206	162
	Lateral	1805	2.5	1.2	14	25	97	242
	AP-oblique	527	1.7	2.2	11	13	108	147
Chest	PA	2.9	0.20	0.25	0.42	1.4	0.48	0.052
	Lateral	12	2.1	2.8	4.2	4.2	0.74	0.12
	PA-oblique	2.3	0.097	0.37	0.17	1.0	0.45	0.036
Abdomen	AP	209	0.59	0.93	3.9	3.8	119	68
Pelvis	AP	147	0.15	0.24	0.72	0.088	21	38
Gallbladder	PA	118	0.18	0.11	1.0	3.6	25	38
	PA-oblique	162	0.12	0.074	0.64	3.8	57	27
Chest (Tomo)	AP	191	1.4	1.7	79	19	19	0.33

Tomo: Tomography.

Table V. Example of dosimetry (neck radiography, anterior-posterior projection)

Position ^b	Measured values (10^{-2} mGy/mAs) ^a					(UC) ^c
	No. 1	No. 2	No. 3	No. 4	Average	
1	1.16	1.18	1.12	1.11	1.14	(0.18)
2	1.24	1.21	1.25	1.24	1.24	(0.19)
3	2.92	2.89	2.89	2.87	2.89	(0.43)
4	2.50	2.40	2.54	2.45	2.47	(0.38)
5	2.97	2.98	3.03	2.95	2.98	(0.45)
6	4.27	4.48	4.51	4.27	4.38	(0.70)
7	4.48	4.67	4.72	4.59	4.62	(0.71)
8	1.63	1.66	1.88	1.93	1.78	(0.36)
9	2.17	2.00	2.10	2.07	2.09	(0.34)
10	0.231	0.221	0.249	0.227	0.232	(0.039)
11	0.266	0.246	0.271	0.264	0.262	(0.043)
12	0.0352	0.0346	0.0369	0.0363	0.0358	(0.0063)
13	0.0539	0.0522	0.0525	0.0530	0.0529	(0.0090)
14	0.0521	0.050	0.051	0.0516	0.0510	(0.0087)
15	0.0393	0.0383	0.0394	0.0385	0.0389	(0.0066)
16	0.0418	0.0400	0.0430	0.0413	0.0415	(0.0073)
17	0.0540	0.0535	0.0547	0.0527	0.0537	(0.0092)
18	0.0479	0.0449	0.0493	0.0473	0.0474	(0.0085)
19	0.0524	0.0535	0.0576	0.0579	0.0554	(0.0104)
20	0.0491	0.0482	0.0476	0.0471	0.0480	(0.0082)
21	0.0382	0.0385	0.0389	0.0403	0.0390	(0.0068)
22	0.0199	0.0190	0.0210	0.0203	0.0201	(0.0036)
23	0.0210	0.0205	0.0218	0.0219	0.0213	(0.0038)
24	0.00214	0.00206	0.00223	0.00215	0.00215	(0.00049)
25	0.00162	0.00172	0.00188	0.00167	0.00172	(0.00034)
26	0.00184	0.00199	0.00196	0.00182	0.00190	(0.00035)
27	0.00045	0.00041	0.00058	0.00053	0.00049	(0.00014)
28	0.00023	0.00056	0.00063	0.00043	0.00046	(0.00023)
29	0.00023	0.00045	0.00051	0.00045	0.00041	(0.00017)
30	5.37	5.32	5.47	5.59	5.44	(0.94)

^aPositions 1–7, 8–29, and 30 were irradiated using 200 mAs, 1000 mAs and 100 mAs, respectively. The focus–film distance was 100 cm. The other technical factors were the same as those shown in Table II. The output of the X-ray equipment used for neck radiography was different from that for experimentation. Doses shown were not adjusted for differences in output and focus–film distance.

^bSee Table I.

^cUncertainty.

according to the physical stature of each AHS participant. Antoku et al (1972) investigated the depth–dose curves in a human phantom in the case of chest radiography. For example, for radiography with posterior–anterior (PA) exposure, an FFD of 183 cm and a tube voltage of 100 kVp, the radiation absorbed dose at a depth of 15 cm was about half that at a 10 cm depth, provided the exposure time was the same. The exposure time for a body thickness of 30 cm is twice that for a body thickness of 20 cm at RERF. The active bone marrow dose was therefore approximately the same in both cases. However, the organ doses near the body surface cannot be estimated without taking into consideration the body thickness and exposure time. For each radiological examination at RERF, the body thickness at the examination site and the exposure time have been recorded routinely. Radiation absorbed doses for each examination can therefore be estimated retrospectively using these recorded data.

Discussion

Hashizume and Maruyama (1979) reported several organ doses while using average technical factors for diagnostic X-ray examinations performed in Japan. These are shown in Table VII along with estimates in the current study for chest and abdominal radiography. All doses were averaged by weighting the frequency of each exposure and projection used at RERF and elsewhere in Japan. The technical factors including the exposure directions used in Hiroshima and Nagasaki medical institutions were investigated by Antoku et al (1986). At RERF, abdominal radiography involved mainly the anterior–posterior (AP) projection and chest radiography involved mainly PA and lateral projections.

The thyroid gland, lung and breast doses during chest radiography agree with those reported by others (Hashizume & Maruyama, 1979). However, large discrepancies were observed among thyroid gland and breast doses during abdominal radiography. Of course,

these organs are located far from the abdominal exposure field. The size and location of the field in question strongly influence the scattered X-ray doses to these organs. Hashizume and Maruyama (1979) also used an Alderson Rando human female phantom such as was used in the present study. The dosimeter that was used in the study by Hashizume and Maruyama (1979) included a cylindrical air chamber, 2 cm in diameter and 4 cm in length. Thus the chamber was relatively large for studying the doses to the breast and thyroid gland, and it therefore seems to have been inferior to the TLDs that were used in the present study.

The National Council on Radiation Protection and Measurements (NCRP) (1968) published average exposure rates produced by diagnostic X-ray equipment. By using the average exposure rates and the present data for scattered X rays (Table VI), surface doses for chest and abdomen examinations were estimated to be approximately 0.18 and 3.2 mGy, respectively. These estimates compare well with the present values (Table III). The outputs of the equipment used for these radiological examinations at RERF therefore agreed with the average output published by NCRP (1968).

The cumulative organ doses received at RERF by a female AHS participant during her radiological examinations are shown in Fig. 4. This subject's physical stature (chest thickness of 19 cm) was not taken into consideration. Data obtained by Antoku and Russell (1971) were used for estimating doses to the active bone marrow and gonads. This AHS subject had received many abdominal examinations including upper GI series; therefore, her stomach and colon doses were relatively high.

Doses received during radiological examinations at RERF can thus be similarly estimated for all AHS participants. Information concerning the body sites examined, the exposures received and technical factors used at other institutions has been obtained during interviews of AHS participants at ABCC/RERF, and all such information has been documented and coded. The organ doses can then be estimated from dosimetry results based on X-ray exposure factors used in

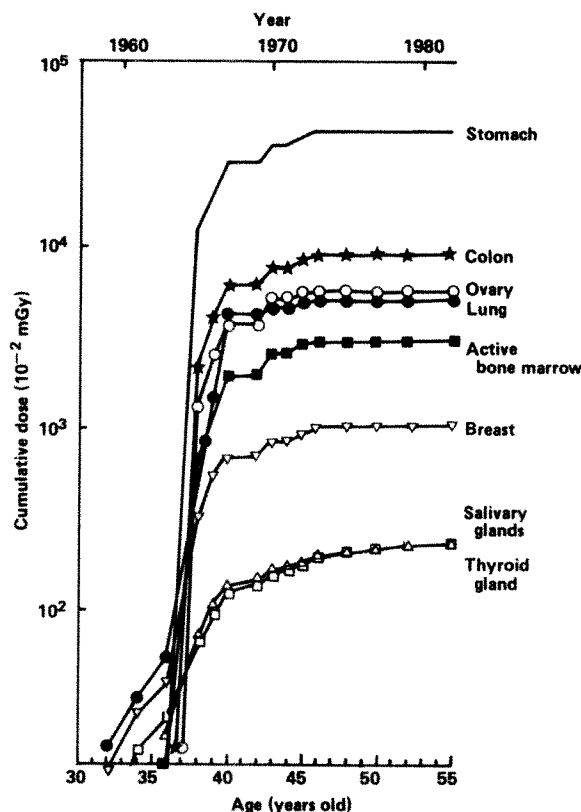


Figure 4. Cumulative organ doses from radiography at ABCC/RERF; a sample estimation. Cumulated organ doses received by an AHS participant (MF # 339524, female) since November 1959, and the date of her initial ABCC/RERF radiological examination, including ovary, active bone marrow, salivary glands, thyroid gland, breast, lung, stomach and colon doses.

Hiroshima and Nagasaki hospitals and clinics (Sawada et al, 1979).

Organ dose estimates for X-ray examinations of AHS subjects received outside RERF are being reported separately (Kato et al, 1990).

Table VI. Scattered X-ray contribution to surface doses

Tube voltage	Exposure (10^{-7} C/kg)	
	Direct X rays	Direct + scattered X rays
80	390	599
100	653	1045
120	957	1504

Note: X-ray exposure factors were as follows: a $17\text{ cm} \times 17\text{ cm}$ irradiation field, a 100 cm focus-ionization chamber distance, 100 kVp tube voltage and a 100 mAs of exposure time multiplied by current. Scattered X rays were caused by a $17\text{ cm} \times 17\text{ cm} \times 15\text{ cm}$ Mix-D block phantom placed behind the ionization chamber.

Table VII. Doses from chest and abdominal radiography

Organ	Absorbed doses (10^{-2} mGy)	
	Present study	Hashizume & Maruyama (1979)
Chest		
Thyroid gland	4.6	5
Lung	18.9	20
Breast	6.9	6.8
Abdomen		
Thyroid gland	1.3	0.3
Lung	5.6	5
Breast	5.5	15

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Organ doses to atomic bomb survivors during photofluorography, fluoroscopy and computed tomography

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Abstract. Doses to the salivary glands, thyroid gland, breast, lung, stomach and colon during mass radiological gastric screening, mass radiographic chest screening, upper gastrointestinal series and computed tomography were determined by exposing a female human phantom to simulated radiological X-ray examinations as performed in community hospitals. The doses were measured using thermoluminescent dosimeters, and the results will be used to document organ doses received by participants in the Atomic Bomb Casualty Commission/Radiation Effects Research Foundation Adult Health Study.

At the Radiation Effects Research Foundation (RERF), the medical X-ray doses received by participants in the Adult Health Study (AHS) have been routinely documented to facilitate the evaluation of any late atomic bomb (A-bomb) radiation effects in the low-dose region (Ihno & Russell, 1963).

Owing to the high incidence of gastric cancer in Japan, mass radiological gastric screening has been widely used for its early detection. In addition, mass radiographic chest screening is still frequently conducted in Japan. Thus, many healthy people receive these examinations, and these examinations contribute to the cumulative doses of many AHS participants. In Japan, examinations such as fluoroscopy during upper gastrointestinal (GI) series and computed tomography (CT) are generally conducted only when indicated by symptoms, physical signs and/or abnormal results of laboratory examinations. These radiological procedures constitute a high risk because of the relatively high radiation doses they deliver per examination.

Estimating organ doses received by patients during such examinations is essential, particularly for RERF subjects. In the present study, dose to the salivary glands, thyroid gland, breast, lung, stomach and colon facilitates efforts to determine the role of medical X rays in the development of various cancers and any other abnormalities among AHS participants. Doses to the active bone marrow and gonads during mass radiological gastric screening and upper GI series have

already been estimated (Takeshita et al, 1972; Antoku et al, 1980; Antoku et al, 1986).

The results reported here will be used for estimating and documenting organ doses based on the responses of AHS participants who were interviewed about their previous medical X-ray examinations.

Materials and methods

Experimental equipment

The X-ray equipment used in this study included (A) a Toshiba DC-15K X-ray tomography unit (Toshiba Medical Systems, Tokyo), (B) a Toshiba Model DTP-OD photofluorography and fluoroscopy unit, (C) a Hitachi Model DR-125-22 TV photofluorography and fluoroscopy unit with an overtable tube (Hitachi Medical Corporation, Tokyo), and (D) a Siemens Somatic Model DRH CT unit (Siemens, Erlangen, Germany).

To simulate X-ray examinations in community hospitals and clinics, an Alderson Rando adult human female phantom (Alderson Research Laboratories, Stamford, USA) was exposed to a variety of X-ray examinations using the above equipment. The phantom was used to simulate an average Japanese adult male and female. Thermoluminescent dosimeters (MSO-S, Kasei Optonix, Odawara, Japan) (TLDs) were used to measure doses to the phantom. The sites where the TLDs were inserted have been described in a previous report (Kato et al, 1989b). Thermoluminescence was measured using a 2000A Thermoluminescence Readout System and a 2000B Automatic Integrating Picoammeter (Harshaw/Nuclear Systems, Cleveland, USA). The coefficient for converting thermolumines-

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Table I. Organ doses during mass radiological gastric screening (unit: 10^{-2} mGy per examination)

Organ	Doses measured for II-TV type ^a			Dose estimated for mirror camera type ^b	
	Fluoroscopy	Fluorography	Total	Total	UC
Salivary glands	0.078	0.15	0.23	1.1	(0.6)
Thyroid gland	0.29	0.19	0.48	2.2	(1.2)
Breast	1.7	0.64	2.3	11.0	(5.4)
Lung	2.8	0.54	3.3	15.2	(7.4)
Stomach	96	95	191	874	(424)
Colon	63	64	127	584	(283)
Gonad (female)	12	21	33	152	(74)

^aDoses are from 35-second total fluoroscopy for positioning and six-film fluorography. Technical factors: focus-to-screen distance 82 cm; added filter 2.9 mm Al; irradiation field 9 inch diameter, automatic control of tube voltage.

^bMean output of mirror-camera-type apparatus with fluoroscreen was assumed to be 4.6 ± 1.9 times that for the machine used in the present study (Antoku et al, 1980).

UC: uncertainty.

cence to exposure was obtained by simultaneously irradiating the detectors and the Exradin A2 Shonka-Wyckoff chambers using the X-ray equipment (described in (A) above) (Kato et al, 1989a). Regardless of tube voltage, 34 (Gy kg/C) was used as the coefficient for converting exposure to absorbed dose. This conversion factor is appropriate for 30–50 keV photons in muscle (International Commission on Radiation Units and Measurements (ICRU), 1979), allowing 7% uncertainty.

Results

Mass radiological gastric screening

The apparatus studied is described in (B) above, and it was used for mass gastric screening. It was equipped with an image-intensifier (II) and a closed-circuit television (II-TV) and a pulse regulator for delivering X rays; however, the present study was conducted without operating the pulse regulator. The resulting measurements are shown in Table I. Experiments were conducted by using: (i) fluoroscopy only for positioning the examinee before each radiographic exposure and (ii) fluoroscopy combined with photofluorographic filming.

Mass radiological chest screening

The output, X-ray quality, and doses incurred using chest photofluorography apparatus used in Hiroshima have already been reported by Antoku et al (1972). In the present study, organ doses were estimated based on the results of that investigation and by phantom dosimetry using equipment (A) (transformer-type apparatus). The results obtained are shown in Table II.

Upper GI series

The upper GI series examinations were simulated using X-ray II-TV type apparatus (described in (C) above). Three radiologists conducted examinations of the human phantom using their own techniques. During

a 1974 investigation of hospital records of medical X-ray examinations, the average fluoroscopy time was found to be 4.5 minutes, and the average number of spot radiographs was 14 in Hiroshima and Nagasaki (Antoku et al, 1986). The organ doses per examination using average technical exposure factors are shown in Table III. Surface and active bone marrow doses were 14.90 and 1.75 mGy/examination, respectively.

CT examinations

Examination sites were categorized as those of the head, chest, upper and lower portions of the abdomen, and the entire abdomen. Whole-body CT apparatus [equipment (D)] was used to "examine" the human phantom, employing the technical factors that were used in practice. Active bone marrow doses were measured at 14 locations in the active bone marrow, as shown in Table IV. As with the other organs, the mean active bone marrow doses were calculated by compartmentalizing the bone marrow so that each resulting

Table II. Organ doses during mass radiographic chest screening

Organ	Measured dose-rate (10^{-2} mGy/mAs)	Dose per examination ^a (10^{-2} mGy)
Salivary glands	0.039	5.5 (2.0) ^b
Thyroid gland	0.048	6.8 (2.5)
Breast	0.28	40 (15)
Lung	1.2	165 (61)
Stomach	0.0038	0.54 (0.23)
Colon	0.011	1.6 (0.6)

^aDoses per examination were adjusted so that the surface dose was 6.46 ± 2.31 mGy, the average dose obtained by Antoku et al (1972). The measured surface dose-rate was 4.6×10^{-2} mGy/mAs.

^bUncertainty is indicated in parentheses.

Table III. Organ doses during upper GI series examinations (unit: 10^{-2} mGy per examination)

Organ	Measured doses ^a				Dose calculated ^b
	A	B	C	Average	
Salivary glands	0.64	20	0.77	6.8	9.3 (0-20) ^c
Thyroid gland	0.95	46	1.1	16	22 (0-48)
Breast	40	153	28	74	102 (42)
Lung	22	103	27	51	70 (29)
Stomach	443	953	370	589	813 (228)
Colon	120	258	195	191	264 (137)
Gonad (female)	7.6	36	80	41	56 (0-115)
Time (minutes)	1.3	5.5	0.8	2.6	4.5
Number of spot radiographs	20	15	13	16	14

^aExaminations were performed by three radiologists: A, B, and C.

^bDoses for II-TV-type apparatus. Technical factors are averages for Hiroshima and Nagasaki (Antoku et al, 1986). In the present study, surface dose-rates for fluoroscopy and spot radiography in the fixed irradiation field were 4.42 mGy/min and 0.54 mGy/spot radiograph, respectively. The doses for the average technical factors were calculated using these experimental data, assuming the dose distribution from fluoroscopy was the same as that from spot radiography.

^cUncertainty is indicated in parentheses. The uncertainties of salivary glands, thyroid gland and gonad doses are expressed as the dose regions.

portion contained one location for TLD measurement. This allowed a mean TLD value weighted by the mass of each part to be used to determine absorbed doses. The total weight of the active bone marrow was considered to be 1.0466 kg, based on the study by Russell et al (1966). Characteristics of the equipment and the technical factors common to all examinations are shown in Table V. Doses resulting from topography conducted before scanning, were less than one-tenth those from scanning. Table VI shows doses per examination, including topography.

Discussion

Mass radiological gastric screening

Mass gastric screening has been widely used in Japan since the mid-1960s, beginning with the use of mirror-

camera type apparatus. However, II-TV units have been popular since 1970.

According to Antoku et al (1980), under average conditions for normal persons, the female gonadal dose during mass gastric screening using an II-TV unit was 0.16 mGy per examination in which 5.7 fluorography

Table V. Computed tomography exposure factors of equipment (D) (Siemens Somatic model DRH)

Specifications

Added filters: 2.2 mm Al, 0.2 mm Cu
Focus size: 1.6 mm × 1.6 mm
Distance between focus and centre of the gantry: 70 cm
Number of detectors: 704
Focus-to-detector distance: 113.5 cm
Effective X-ray range: 51 cm diameter
Gradient of gantry: $\pm 25^\circ$

Exposure factors

Scan slice width: 8 mm
Scan feed width: 8 mm
Slice number/scan: 1
Scan time: 5 seconds
mAs/scan: 410 mAs
Topograph slice width: 2 mm
Topograph time: 7 seconds
mAs/topograph: 220 mAs
Tube voltage: 120 kVp (examination of the head)
125 kVp (organs other than the head)
Number and site of scans:
14 scans, brain (CT examination of the head)
35 scans, lung (CT examination of the chest)
19 scans, T10-L3 (CT examination of the upper abdomen)
25 scans between L3 and L4 to symphysis pubica (CT examination of the lower abdomen)
48 scans from T10 to symphysis pubica (CT examination of the entire abdomen)

Table IV. Dose measurement sites in the active bone marrow

No.	Measurement site
1	Sella turcica
2	Cervical spine/4
3	Thoracic spine/6
4	Rib/4
5	Rib/4
6	Rib/4
7	Rib/6
8	Rib/6
9	Rib/6
10	Rib/8
11	Rib/8
12	Rib/8
13	Thoracic spine/12
14	Lumbar spine/3

Table VI. Organ doses during CT

Organ	Doses (mGy per examination)				
	Head	Chest	Upper abdomen	Lower abdomen	Whole abdomen
Salivary glands	3.16 (1.45) ^a	4.60	0.34 (0.45)	0.07 (0.04)	0.31
Thyroid	1.65 (9.60)	6.67	0.47 (0.54)	0.07 (0.04)	0.40
Breast	0.19 (0.15)	48.09	2.97 (14.80)	0.57 (0.21)	2.96
Lung	0.47 (0.18)	42.97	6.99 (6.80)	0.36 (0.11)	6.66
Stomach	—	5.32	35.33 (7.60)	2.66 (0.43)	42.06
Colon	—	0.83	5.39 (0.26)	17.00 (12.10)	38.14
Gonads (female)	—	0.20	0.43 (0.18)	24.18 (9.50)	25.40
Active bone marrow	4.08 (1.41)	7.28	5.56 (1.74)	4.59 (2.60)	10.32
Surface ^b	41.98	47.59	45.03	37.17	46.97

^aThe doses measured by Nishizawa et al (1981) are shown in parentheses. The values in parentheses for salivary glands are those to the sublingual gland. Eight scans per examination were used for every examination site. Seven CT scanners were used with tube voltages ranging from 120 to 140 kVp, slice thicknesses of 10–13 mm and scan times of 4.5–105 seconds.

^bSurface doses represent doses at the surface in the centre of the examination site (see Table V).

films were exposed and a total of 49 seconds fluoroscopy exposure was used for positioning. In the present study, a dose of 0.33 ± 0.09 mGy per examination was obtained. This is about one-fourth the 1.40 mGy mean for Hiroshima City obtained by Antoku et al (1980). The national average obtained by Hashizume et al (1977) for the mean female gonadal dose was 1.50 mGy when mirror-camera apparatus was used. In the present study, no experiment was performed to measure doses received during the use of a mirror-camera apparatus with fluoroscreen. The active bone marrow dose from fluoroscopy used only for positioning the patient was about 4.6 times less than that when a mirror-camera apparatus with fluoroscreen was used (Antoku et al, 1980).

Mass radiographic chest screening

Chest photofluorography units were categorized as condenser and transformer types. Both types differed markedly in characteristics, although Antoku et al (1972) observed little difference with respect to the surface and bone marrow doses incurred. However, doses to the gonads were slightly higher when using the transformer-type units, for which beam collimation was frequently inadequate (Antoku et al, 1972). The doses shown in Table II are, therefore, not precisely correct for examinations performed with inadequate collimation. The collimation techniques have since been improved. Thus, the doses obtained in the present study are considered conservative, regardless of apparatus type, providing the beam collimation is sufficient.

Upper GI series

Fluoroscopy techniques vary between medical institutions and among physicians. Fluoroscopy time and the number of spot radiographs used likewise differ according to the examinees' health status. In 1969, Takeshita et al (1972) showed that mean bone marrow doses received during upper GI series performed by

radiologists using X-ray TV fluoroscopy varied widely—from 0.56 to 6.6 mGy per examination. The present estimates (Table III) are for X-ray TV fluoroscopy using the techniques employed at major hospitals. As shown in this table, the errors in estimates for individual examinations appear to be relatively large. The active bone marrow doses obtained agree with those estimated by Antoku et al (1986). The thyroid and stomach doses reported by Yamamori et al (1988) are larger than those obtained in the present study, but do not exceed by twice the values of the present study (Table VII). However, the mean bone marrow dose obtained by Yamamori et al (1988) was 15.20 mGy per examination, which was six times greater than the 2.59 mGy per examination estimated from the present results for the fluoroscopy times and numbers of spot radiographs used by Yamamori et al (1988). The active bone marrow dose by the latter was greater than the maximum surface dose obtained in the present study.

In Report 33 of the National Council on Radiation Protection and Measurements (NCRP, 1968), the air exposure rate at the anterior surface of the human phantom is reportedly approximately 1.55×10^{-4} C/(kg min) during fluoroscopy when the exposure field is

Table VII. Comparison of organ doses during upper GI series

Organ	Doses (mGy per examination) ^a	
	Calculated ^b	Reported ^c
Thyroid	0–0.70	0.50
Lung	1.04 ± 0.44	5.10
Stomach	12.04 ± 3.37	24.0

^aFluoroscopy time: 7.6 minutes, 13 spot radiographs per examination [used by Yamamori et al (1988)].

^bCalculated from the measured doses shown in Table III.

Calculated without considering differences in output.

^cAfter Yamamori et al (1988).

Table VIII. Doses per scan during CT examinations of the head

Organ	Doses (mGy per scan) ^a	
	Present	Reported ^b
Active bone marrow	0.29 ± 0.10	0.34
Salivary glands	0.23 ± 0.06	0.16 ^c
Thyroid gland	0.12 ± 0.03	0.12
Breast	0.013 ± 0.004	0.022
Lung	0.034 ± 0.011	0.017

^aSee Table VI.^bThe doses were measured by Nishizawa et al (1981) using CT apparatus with a tube voltage of 120 kVp, a tube current of 350 mA, a scan time of 9 seconds, one slice per scan, a gantry diameter of 60 cm, a 2.5 mm Al added filter and a slice thickness of 10 mm.

These factors were similar to those used in the present study.

^cDoses to the sublingual gland.

fixed. The measured exposure rate was 1.29×10^{-4} C/(kg min), thus the present X-ray tube is similar to the standard one. The currently used imaging system permits the use of a long focus-to-screen distance (100 cm). Such relatively large distances are commonly used with recently developed fluoroscopy equipment. Before the advent of the II-TV-type equipment, doses from upper GI series examinations were greater than those shown in Table III. Takeshita et al (1972) showed that 3.02 minute conventional fluoroscopy and 6.6 spot radiographs caused examinees to receive 3 mGy active bone marrow doses, which were three times greater than those of the present study using II-TV-type apparatus, the same fluoroscopy times and same number of spot radiographs.

CT examinations

Table VI shows organ doses incurred during CT examinations, as determined in the present study, and organ doses estimated by Nishizawa et al (1981). Nishizawa et al (1981) assumed that eight scans were made uniformly during examinations of the head and the upper and lower portions of the abdomen. However, in the present study 14 scans were made, even for CT of the head. The values obtained by Nishizawa et al (1981) are therefore generally lower than those obtained in the present study. However, the reported estimates of thyroid doses during head CT, and breast doses during CT of the upper portion of the abdomen are much higher than those obtained in the present study. The average thyroid dose from CT head scans obtained by Nishizawa et al (1981) is greater than each of the measured values. Also the breast dose from upper abdominal scans by Nishizawa et al (1981) is greater than the other doses from the same scan, probably because the scan position used by Nishizawa et al (1981) differed from the present one. Table VIII shows the organ doses per scan during head CT, as obtained in the present

study and those obtained by Nishizawa et al (1981). Exposures per scan were similar when examinations were conducted under similar conditions of exposures and using similar types of equipment, as indicated in Table VIII.

The active bone marrow dose incurred during CT is relatively high because the tube voltage is also relatively high (120 kVp), and the body is irradiated in nearly all projections. In the present study, doses to the bone marrow within the irradiation field were more than half the doses to the body surface within that field. In addition to this, doses differed greatly for exposures inside, as compared with those outside the exposure field, because a relatively small beam was used. For example, relatively high doses such as 50 mGy were incurred to a rib per examination during chest CT, and 30 mGy to the 12th thoracic and third lumbar vertebrae per examination during CT of the entire abdomen. The active bone marrow dose during CT of the entire abdomen was about 60 times greater than the active bone marrow dose during antero-posterior (AP) radiography of the abdomen using technical factors employed at RERF (Antoku & Russell, 1971). Although CT scanning has recently become widely used, it should be used carefully, because it exposes examinees to very high radiation doses.

Data obtained in the present study will be used to document medical X-ray doses received by subjects who reported they were exposed to these radiological examinations.

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Calibration of a Microselectron HDR iridium 192 source

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Abstract. A method for the calibration of the output, in terms of an air kerma rate, of the high activity miniature iridium 192 sources used in the Microselectron HDR afterloading unit is described. An air kerma rate is measured using a calibrated thimble chamber in an "in-air" calibration jig. The results are compared with an air kerma rate derived from the manufacturer's test certificate. In some cases, the ionization chamber measurements have been followed by a further calibration check using thermoluminescent dosimetry. Other checks carried out when a new source is received are also briefly described.

The Microselectron HDR (Nucletron Trading Ltd, Tarporley, Cheshire) is a remote afterloading system for intraluminal, interstitial and intracavitary therapy. The unit contains a source of iridium 192 of nominal activity 370 GBq (10 Ci). The early sources had an active length of 3.5 mm; more recent sources have an active length of 4.5 mm. The diameter of the source capsule is 0.9 mm. The source is mounted on the end of a flexible drive cable which is driven by a stepper motor into an applicator. Various applicators are available; the one used in this work was the bronchial applicator which is a flexible plastic applicator of external diameter 1.9 mm.

The treatment unit can be programmed to treat up to 18 channels sequentially; each channel is made up of a series of 48 possible dwell positions of the source, each position being separated by 2.5 mm, giving a treatment length of up to 120 mm. A recent upgrading of the control software now allows the option of 5.0 mm dwell position separation, giving a treatment length of up to 240 mm. This option was not available when the work described here was carried out. The length of time to be spent in each dwell position is programmed from the keyboard on the control unit. On each occasion that an exposure is initiated, before the source is transferred, a check cable is run into the applicator system, and returned, to check for obstructions.

Iridium 192 has a half-life of 74 days, and the unit therefore requires a source change every 3 months otherwise treatment times become unacceptably long. Therefore easily reproducible and convenient arrangements to measure source output and check the source positioning are required.

Calibration method

In order to simplify the experimental arrangement, and to keep to a minimum any corrections for attenuation in plastics or other materials, it was decided to perform the measurements in air. The intention was to determine an air kerma rate at a known distance from the source.

A Perspex jig was constructed, consisting of a central Perspex tube machined to fit accurately around the ionization chamber and stem. The Perspex had a wall thickness of 3 mm in the region of the chamber. Parallel to this tube were four thin walled Perspex tubes, of internal diameter such that they would accept a bronchus applicator of diameter 1.9 mm. The distance of each of these tubes from the central axis of the jig and also therefore from the central axis of the ionization chamber was 50 mm. The overall dimensions of the jig were 130 mm × 130 mm × 165 mm. The device is shown in Fig. 1.

The dosimeter system consisted of a 0.3 cm³ thimble chamber, type PTW 23332, and a PTW SN4 electrometer.

The jig and chamber were set up on a 100 mm thick Styrofoam block to reduce the effect of scatter from the table top. They were positioned so that the tubes for supporting the ion chamber and applicators were horizontal. Measurements done on various thicknesses of Styrofoam block showed no significant differences, indicating that a thickness of 100 mm was sufficient to reduce the effect of scatter from the table top to acceptable levels. The ion chamber was approximately 1 m from the floor of the room, and 3 m from the nearest wall. Measurements taken with the apparatus submerged in a water phantom, when corrected for absorption and scatter by the method of Meisberger et al (1968), gave results insignificantly different from the "in air" measurements described here. The measurements done in air were more convenient to undertake, and as the results were comparable this was the method of choice. It was concluded that the effect of scatter from the jig itself, in the "in air" situation, was minimal, otherwise the agreement between the two methods would not have been so good. A bronchus applicator was inserted into one of the four applicator tube holders of the jig and connected to the treatment unit. The optimum dwell position, that is the one closest to a line at right angles to the axis of the chamber and opposite

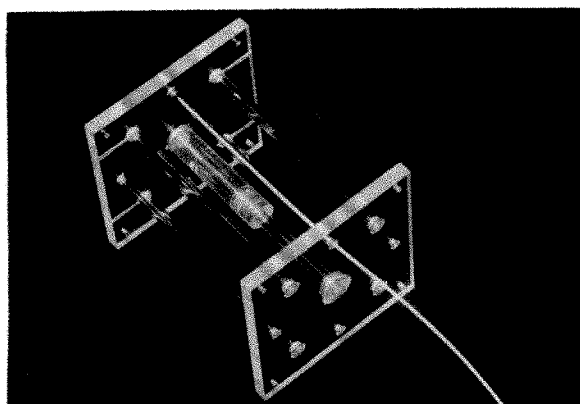


Figure 1. An in-air calibration jig for the calibration of a microselectron HDR source.

the centre of the chamber, was found by taking electrometer readings for a number of dwell positions and finding the dwell position that gave the maximum reading. Using this dwell position for the rest of the procedure, 120 s exposure readings were taken with the source in each of the four applicator tube holders around the chamber. Repeat measurements were taken for each position. The mean of the two readings was then calculated. The arrangement of four applicator positions reduced potential errors from source positioning, irregularities in source geometry, detector geometry, and jig dimensions.

On those occasions where a newly supplied source was being calibrated, rather than a check on a previously calibrated source, the dosimetry equipment would be dismantled, and re-assembled by another physicist who then repeated the calibration. The two independent answers obtained were compared together with the test report before the source was released for clinical use.

Recently, a further calibration check has been carried out. A TLD dosimeter was made up, consisting of a small gelatin capsule of dimensions 13 mm × 5 mm containing 40 mg of lithium fluoride with a Perspex plug filling the rest of the capsule and preventing the formation of an airspace. A capsule was placed in the central tube of the calibration jig in place of the chamber. A suitable exposure time was selected and the capsule was exposed. The process was repeated for each of the four source channels on the jig. The calibration factor for lithium fluoride at cobalt 60 energy was used. The variation in the response of lithium fluoride with energy is flat in this region, and the cobalt 60 calibration factor was used without modification (Fowler & Attix, 1966).

Other checks

In addition to the source calibration, various other checks were performed at regular intervals and particularly when a source had been changed. Three of these checks will be described briefly here.

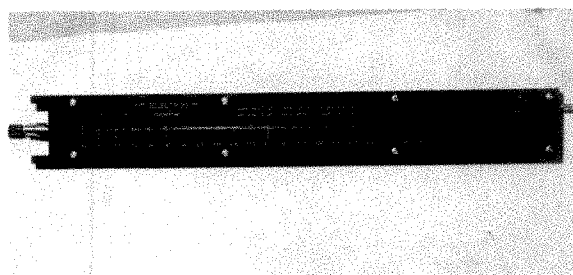


Figure 2. Manufacturers calibration rule for checking source positioning.

- (1) It is important to check that the source goes correctly to a programmed dwell position. To help with this, the manufacturers supply a calibration rule (Fig. 2) which is essentially a transparent catheter alongside a scale graduated in millimetres. The device has a marker wire inside the tubing which is pushed by the source, so that when the source is retracted the position that the source reached can be ascertained. We preferred to view the device with a CCTV system with a zoom lens so that we could check the position of both the check cable and the source in a number of positions as the source stepped along the applicator.
- (2) Within the applicators there is a dead space towards the tip, the length of which may vary from one type of applicator to another, beyond which the source will not travel. A typical value of this is approximately 8 mm for the gynaecological and bronchial applicators. To investigate the effect of this, autoradiographs were taken. The film used was Kodakline 2586. An applicator was taped to the film packet and various dwell positions, including the end position, programmed and exposed. The processed films were analysed by the use of a scanning microdensitometer. The scans allowed both the checking of the dead space and the checking of the distances between the dwell positions. This procedure was repeated for all applicator types. Figure 3 shows an example of a scan from the microdensitometer.

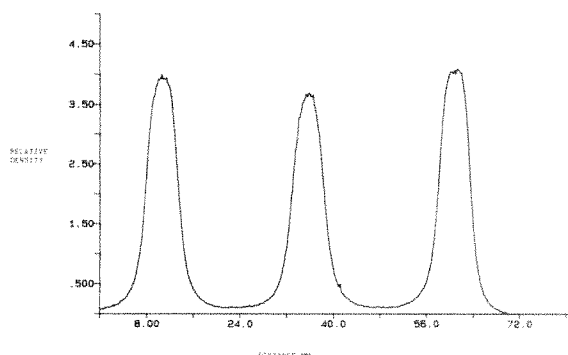


Figure 3. Microdensitometer scan showing three source positions in a bronchial applicator.

- (3) At the end of a series of measurements or checks, the applicator that had been used was checked for contamination by iridium 192. Although the new sources were supplied with a wipe test report, we preferred to repeat the test ourselves. An actual wipe test on a source that has been loaded into the unit is not possible, but it is likely that if a source were leaking some activity would transfer to the applicator.

Calculation of results

The ionization chamber and electrometer air kerma calibration factor was determined by interpolation between values for 115 keV (HVL 2.1 mm Cu) and 661 keV (caesium 137) assuming an average γ -ray energy for iridium 192 of 370 keV. These factors were obtained by comparison with a secondary standard instrument which had been calibrated at these two energies by the National Physical Laboratory, as part of its regular calibration procedure. The use of this interpolation method is described by Ezzell (1989) and Goetsch and Attix (1989).

The effects of dose gradient and the proximity of the chamber to the source were considered. Even though the chamber was placed at the centre of an arrangement of four source positions, because the exposure was made by a single source, which moved from one place to another, rather than by an arrangement of sources that were exposed simultaneously, a dose gradient did exist across the chamber. Kondo and Randolph (1960) have analysed this situation and their results suggest that for an ionization chamber of the type that we used, that is 6 mm diameter, 18 mm long at 50 mm from the source, the chamber readings should be increased by 1%. The results presented here have been corrected by this amount.

The timer of the Microselectron HDR unit was used to control the timing of the calibration exposures. This means that each measurement taken includes a contribution received during the transfer of the source from the safe to the dwell position, and back to the safe, at the beginning and end of each exposure. The magnitude of this component was assessed by taking readings with programmed dwell times of 0.1, 0.2, 0.3 and 0.4 s and extrapolating down to a zero exposure time. Typically the amount that had to be subtracted from each reading was about 0.3% of the reading. An alternative method would be to use a separate timer to time the periods of measurement of the electrometer, and so eliminate the transit dose.

The effect of the 3 mm Perspex wall thickness around the detector was investigated in the following way. Measurements were taken, using the same ionization chamber and source, in the same geometrical arrangement as the calibration, with thicknesses of Perspex around the chamber of zero, 3 mm and 6 mm. Each successive addition of 3 mm Perspex reduced the reading on the electrometer by 2%. It was therefore assumed that the 3 mm of Perspex in the calibration jig reduced the reading by 2% and the actual readings

obtained for the calibration exposures were therefore increased by this amount. The assumption was made that full electronic equilibrium had been obtained for this chamber. For X-rays up to 500 keV, the maximum electron build-up is established by 1 mm or less of chamber wall (NCRP, 1981). All readings were corrected to standard temperature and pressure, namely 293 K and 1013 mbar (760 mmHg).

In order to show more clearly the calculations associated with the calibration, those relevant to the source identified as "G", which has a reference date of 8 September 1989, are shown in Table I. There were two sets of figures throughout, except at the end when the two sets were averaged. The two sets were derived from the readings taken independently by the two operators, on separate occasions. The allowance for the transit dose was made by the method just described, and values of 0.31 and 0.29 were determined on the two occasions. The Perspex wall correction factor and the dose gradient correction factor were taken to be 1.02 and 1.01, as described previously.

The dosimeter readings were taken during exposures of the source, in its predetermined optimum dwell position, for a period of 120 s, in each of the four jig positions. Ideally these results should have been identical. In practice they were not; some variations in the pattern of the four readings were seen from one occasion to another, and the deviation from constancy was seen to be up to about 5%. The variation in reading was probably due to the effects of the catheter "snaking" in its applicator, the effect of difference in scatter from one position to another or differences in sensitivity of the chamber when being exposed from different directions. These areas need to be investigated further. These readings were then corrected for dose gradient effects, transit dose, and Perspex wall attenuation, and the result was recorded.

In order to express the result as an air kerma rate at 1 m the reading (R) needs to be multiplied by the dosimeter calibration factor and a number of other factors:

$$\begin{aligned} \text{Air kerma rate at 1 m (Gy/h)} = \\ R \times \text{calibration factor} \times \text{distance factor} \times \\ \text{time factor} \times \text{temperature correction} \times \\ \text{pressure correction.} \end{aligned}$$

In the case of the "Measurement 1", this leads to an air kerma rate at 1 m of

$$\frac{91.28 \times 5.7 \times 10^{-3} \times 50^2 \times 3600 \times 294 \times 760}{1000^2 \times 120 \times 293 \times 745} \text{ Gy/h} = 0.0399 \text{ Gy/h,}$$

and for "Measurement 2", the air kerma rate at 1 m is given by

$$\frac{90.74 \times 5.7 \times 10^{-3} \times 50^2 \times 3600 \times 294 \times 760}{1000^2 \times 120 \times 293 \times 746} \text{ Gy/h} = 0.0397 \text{ Gy/h.}$$

The two sets of measurements were taken approximately 4 h apart; the radioactive decay of iridium 192 in

Table I. Experimental results for source "G"

	Measurement 1	Measurement 2
Reference date	8 September 1989	8 September 1989
Measurement date	15 September 1989	15 September 1989
Temperature	294 K	294 K
Atmospheric pressure	745 mmHg	746 mmHg
Optimum dwell position	27	27
Dosemeter calibration factor (air kerma)	5.7×10^{-3} Gy per digit	5.7×10^{-3} Gy per digit
Transit dose correction (<i>A</i>)	0.31	0.29
Perspex wall correction (<i>B</i>)	1.02	1.02
Dose gradient correction (<i>C</i>)	1.01	1.01
Dosemeter readings, 120 s (R1 and R2)	89.51, 89.61 91.03, 91.24 87.34, 87.25 87.60, 87.69	88.52, 88.64 90.06, 89.99 88.10, 88.03 86.86, 86.73
Mean corrected readings		
$R_c = [\frac{1}{2}(R1 + R2) - A]BC$	91.95 93.57 89.62 89.98	90.96 92.45 90.43 89.12
$\bar{R} = R_c/4$	91.28	90.74
Air kerma rate, at 1 m (Gy/h), see text	0.0399	0.0397
Mean of measurements 1 and 2 (Gy/h)		0.0398
Decay factor (7 days)		0.9365
Air kerma rate at 1 m on reference date (Gy/h)		0.0425

this period is approximately 0.15%. The two values of air kerma rate differ by 0.5%, which is presumably due to experimental differences. Table I shows the combination of these two values, and the calculation of an air kerma rate at 1 m on the source reference date, giving an answer of 0.0425 Gy/h.

For comparison, the test certificate from the suppliers states that the source produces an exposure rate at 1 m of 4.66 Rh⁻¹ on 8 September 1989. This is equivalent to

an air kerma rate of 0.0407 Gy/h at 1 m, using a multiplying factor of 8.73×10^{-3} Gy/R. Therefore the ratio of the measured to the test certificate air kerma rate is 1.044.

Results

Table II shows the results of the calibration of eight sources, each received at approximately 3-monthly intervals. It shows, for each source, the air kerma rate at 1 m derived from the manufacturer's test certificate compared with the air kerma rate at 1 m obtained from measurements of the type described above. Both of these are corrected for radioactive decay to the same date, so that they are directly comparable. The final

Table II. Air kerma rates; measured values compared with test report

Source reference	Measured air kerma rate (Gy h ⁻¹ m ²)	Test certificate air kerma rate (Gy h ⁻¹ m ²)	Measured/test certificate
A	0.0349	0.0325	1.074
B	0.0355	0.0366	0.970
C	0.0337	0.0325	1.037
D	0.0372	0.0366	1.016
E	0.0423	0.0422	1.002
F	0.0425	0.0429	0.991
G	0.0425	0.0407	1.044
H	0.0423	0.0402	1.052
Mean ratio			1.023

Table III. TLD results, TLD result compared with expected (based on ion chamber measurements)

Source reference	TLD measured air kerma (Gy)	Expected air kerma (Gy)	Measured/expected
F	1.296	1.263	1.026
G	1.416	1.397	1.014
H	1.252	1.240	1.010
Mean ratio			1.017

column gives the ratio of the measured report value to the test report value.

Table III shows the results of the thermoluminescent dosimetry (TLD) measurements of the three most recent sources.

Discussion

Our intention was to devise a method of absolute calibration of the iridium 192 sources used with the Microselectron HDR, which would be quick and easy to use and yet, of course, would give consistent and reliable results. When, as is the case with this machine, the source needs to be changed every 3 months and the machine is in regular clinical use, the time that it is unavailable needs to be kept to a minimum. Additionally we perform an output check at monthly intervals, in line with the recommendations for γ -beam teletherapy units. This calibration method allows us to do the necessary checks in the minimum amount of time. Typically the treatment unit will be unavailable for about $1\frac{1}{2}$ days at the routine service, source change, and calibration period. The monthly interval checks take about half an hour and can easily be carried out without interfering with clinical use.

Our results have been presented in air kerma rates. This is the quantity obtained from our measuring system using the calibration factor mentioned previously. The source manufacturer's test certificate is expressed in terms of exposure rate in both $\text{R h}^{-1} \text{m}^2$ and $\text{mC h}^{-1} \text{m}^2 \text{kg}^{-1}$, and activity in both GBq and Ci. Our table value of the test report figures is based on the $\text{R h}^{-1} \text{m}^2$ value multiplied by $8.73 \times 10^{-3} \text{ Gy/R}$. The planning system that we use (Nucletron) accepts source data in terms of either activity or air kerma rate. In brachytherapy dosimetry a knowledge of the activity is not necessary if one can calculate the absorbed dose rate at a point from a knowledge of the air kerma rate at some reference distance. In fact the use of the activity can be misleading unless one is certain of the value of exposure rate constant or air kerma rate constant that has been used to derive that activity. If a value different to the one used originally to derive the activity is subsequently used for a dosimetry calculation, an incorrect answer will be obtained.

Table IV. Repeat measurements of air kerma rate. Showing ratio to original measurement, corrected for source decay

Source reference	Remeasured air kerma rate
	Original measured AKR
C	1.000
D	1.006
E	0.993, 1.002
F	1.003
G	0.993, 0.996
Mean ratio	0.999

The degree of agreement between our measurements and the test report values can be seen in Table II. With two exceptions, the measured values are greater than the test report values. Over the eight sources, the mean ratio of measured/test report is 1.023. Overall therefore our calibration method appears to be an effective and reasonably accurate method of calibration as a check on the test report.

The variations from one source to another do however cause some concern. Even if either the manufacturer's technique, or our technique, were incorrect in some way, an approximately equal ratio between measured and test report values for all of the sources would be expected, although it would of course differ from unity. The variations in this ratio, from 1.074 to 0.970, suggest that there is some variation either in the manufacturer's calibration technique or our technique.

Owing to our practice of performing repeat calibration checks at monthly intervals during the useful life of the source we can compare re-measurements of an individual source with the initial calibration measurements and get a measure of the reproducibility of our technique. If our results are consistent and without the larger variations seen in the original calibration of each source, the likelihood is that it is the manufacturer's measurement technique that is the cause of most of the variability rather than ours.

Table IV shows the results of such a comparison. The ratio of our recalibration to our original calibration ranges from 1.006 to 0.996 with a mean of 0.999. Thus our technique is, at least, reproducible, to an extent much better than the original calibrations would suggest. It appears that the manufacturer's calibrations are less reproducible than ours, and we are currently discussing this problem with them.

Table III shows the results of our TLD checks on three recent sources. Although these are measured as an absorbed dose they have been entered in the table as air kerma, to allow comparison with our measurements. The exposure times were chosen to give a suitable dose on the linear part of the lithium fluoride calibration curve. The expected value is the air kerma that would have occurred in the exposure time, using the air kerma rate derived from the ionization chamber measurements. Agreement well within 3% was obtained.

Measurements around brachytherapy sources are not easy. With low dose rate sources there are difficulties with long measurement times and electrometer drift, and steep dose gradients around the source. The high activity source considered here does allow shorter exposure times, and the effect of dose gradients can be reduced by increasing the distance between the source and the chamber, although this does then tend to increase the exposure time. We feel that for this source, a measurement distance of 50 mm provides a reasonable compromise between having a convenient exposure time and small dose gradient effects on the chamber. Other workers have used different source to chamber distances (Ezzell, 1989).

One major difficulty is the choice of calibration

factor, in both the case of the ionization chamber and the TLD. In both cases we have assumed a calibration factor based on a formal calibration of the instrument or substance at a different photon energy, and a knowledge of the properties of the measurement system in the relevant range of photon energies. Whilst we feel this is acceptable, as any change in the factor will be small, it would be preferable to have a factor for the relevant photon energy directly traceable to a standard.

In the case of external beam radiotherapy, protocols exist describing recommended methods for the calibration of radiation beams (HPA, 1983). There is no such protocol for brachytherapy sources, and users of these sources devise their own methods of calibration. With the probable increase in use of such equipment in the future, it is necessary for some standardization of method to take place to ensure consistency of calibration both within a particular radiotherapy centre and between centres.

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Response of the mouse mediastinum to single and fractionated X-rays

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Abstract. The acute oesophageal response, after localized mediastinal irradiation in unanaesthetized mice, was assessed with a sequential, non-invasive and clinically orientated assay. Changes in body weight, after single and fractionated X-ray doses (8 fractions in 8 or 15 days and 4 fractions in 4 or 13 days), were recorded and the nadir of weight loss for each regime was used as the end-point. In our studies, quantal and non-quantal analyses of the weight loss data gave good dose-response relationships. The shapes of the dose-effect curves for single doses, 4F/4 days and 8F/8 days showed a remarkable degree of radioresistance, which became less apparent when the overall time was increased to 13 and 15 days for 4 and 8 fractions, respectively. The α/β values (7–17 Gy) are within the range found for other acutely responding normal tissues. Histopathological changes were also assessed and the structural changes observed in the oesophageal epithelium, after a single dose of 34 Gy or after 46 Gy given as 3F/6 days, correlated with the gross changes observed in body weight.

In clinical radiotherapy the oesophagus must unavoidably be included in the treatment fields of many thoracic tumours. Frequently, the acute oesophageal reaction, accompanied by retrosternal pain, causes the radiotherapist to perform a split-course irradiation often with several weeks rest, or else the reaction may become dose limiting. An increase in overall time and/or a decrease in total dose are both disadvantageous for the outcome of palliative or curative treatments.

Little experimental information is available on the time-dose-fractionation parameters of the oesophagus. Although decreased food intake and body weight loss, after whole thorax irradiation, were shown to be caused primarily by acute and subacute oesophageal damage (Kurohara & Casarett, 1972), animal lethality was chosen subsequently as the end-point for acute oesophagitis (Phillips & Margolis, 1972; Phillips & Ross, 1974; Hornsey & Field, 1979). It was shown that lethality, due to epithelial denudation, occurred over a well defined period of time with dehydration and starvation being the main cause of death in the animals before lung damage became the cause of death (Phillips & Margolis, 1972; Phillips & Ross, 1974). In these studies, however, the whole of the thorax of anaesthetized animals was included in the treatment field. The use of lethality, after total thorax irradiation, to assess the oesophageal response may reflect radiation damage to thoracic structures other than the oesophagus (Michalowski &

Burgin, 1982). Furthermore, as first suggested by Phillips and Ross (1974) and subsequently confirmed by Hornsey and Field (1979), under air-breathing conditions the oesophagus of anaesthetized mice shows a considerable degree of hypoxia which might, however, have been influenced significantly by the use of anaesthesia (Hornsey & Field, 1979).

Non-invasive, sequential, clinically orientated and humane assays are preferable to lethality when monitoring the response of tissues to radiation damage. We have, therefore, further developed the observation of Kurohara and Casarett (1972) and have used weight loss as an end-point for acute oesophageal damage. We have been able to avoid the use of anaesthesia by a suitable mouse-holding jig. To limit the damage to other thoracic structures a small irradiation field, limited to the mediastinal region, was defined. To determine the sensitivity of the oesophagus to dose fractionation, single large or repeated smaller doses of X-rays were given in overall times that were probably shorter (4 fractions in 4 days and 8 fractions in 8 days) or longer (8 fractions in 15 days and 4 fractions in 13 days) than the turnover time of the oesophageal basal cells (Phillips & Ross, 1974).

Materials and methods

Mice

Adult CBA/Gy/BSVS male mice, 12–13 weeks old, with a mean weight range of 32 ± 1.5 g (SD) were used. The animals were weighed just before the first X-ray fraction and on successive days thereafter for a total of 35 days. Four animals were used per dose group.

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Previously, we have shown that weight loss is a sensitive assay for acute oesophageal damage, which gives good dose-response relationships. In that study, body weight data were expressed as the average weight loss over a period of time, or as the weight at nadir, or as quantal data. No difference in the interpretation of the results was found when using any of these three methods of analysis (Marino et al, 1990). In this paper, dose-response curves for either the weight at nadir or for quantized data are presented.

Assays

Weight at nadir. This is the lowest weight attained by an animal after the completion of a fractionation regime and is expressed as a proportion of its initial pre-treatment weight. The mean nadir weight (± 1 SEM) was calculated for each dose group. The nadir was observed at varying times for the different overall treatment durations (Fig. 1 and Table I). After reaching the nadir the mice regained weight, except those receiving the higher radiation doses. Some of these animals died or were killed for humanitarian reasons because of deteriorated general condition and/or signs of respiratory distress. However, only three out of a total of 226 mice showed signs of respiratory impairment over the period in which weight loss was analysed, and the weight changes observed are unlikely to be influenced by radiation damage to the lung. Table I summarizes the time scales for nadir and animal lethality. The weight at nadir, expressed as a proportion of the initial pre-irradiation weight, was plotted against dose as the mean and standard error for the mice in each dose group (four animals per group). The dose-effect curves were determined objectively by non-linear least squares regression, using a generalized logistic function fitted to all the individual measurements for each mouse. Values of isoeffect doses ($\pm 95\%$ confidence limits) were obtained for each curve by back-substitution in the equation fitted to each set of data points by the regression analysis (Joiner et al, 1989) and these were then used to derive the α/β ratio, using the method described by Tucker (1984).

Quantal analysis. The weight at nadir of each mouse, including "dead responders", was expressed as a percentage of the time-matched mean weight of sham-

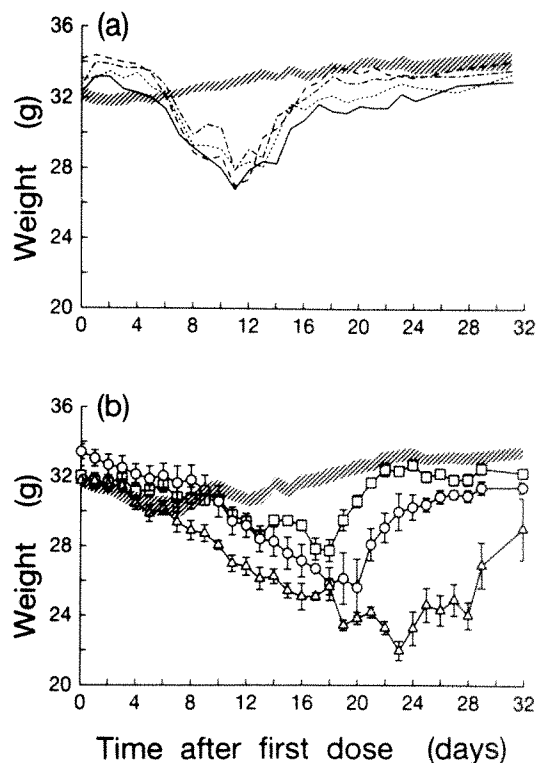


Figure 1. Change in body weight in four CBA male mice after a single dose of 34 Gy (a) and mean weight (± 1 SEM) of mice during and after a course of fractionated X-rays (b) given as 8 fractions in 15 days, to a total dose of 65.70 or 75 Gy ($\square$, $\circ$, $\triangle$, respectively). The hatched areas show the average weight (± 1 SEM) for control mice (eight animals per schedule) sham-irradiated either once (a) or 8 times over 15 days (b).

irradiated controls for each radiation schedule. The mean weight loss of all these animals was 26%. The number of mice whose weight loss was $\geq 26\%$ after the end of a fractionated schedule was determined for each dose group and the resulting quantized data fitted by logit analysis. The same analysis was done for percentage weight loss levels of 25, 27 and 28% of controls (data not shown). Values of α/β were obtained from

Table I. Fractionation schedules, average day of nadir and animal lethality

Number of fractions	X-ray dose per fraction (Gy)	Overall time (days)	Day of nadir (after first dose)	Day of death (after first dose)
1	24-80		11	19
4	13-21.3	4	11	15
4	13-21.3	13	21	23
8	8.13-12.5	8	14	18
8	8.13-12.5	15	21	23
12†	5.83-8.33	12	19	21
12†	5.83-8.33	15	19	21

†Marino et al (1990).

these data using the direct analysis method (Thames et al, 1986).

Histology. The time course for denudation and recovery of the oesophageal epithelium was also determined. Mice were sacrificed on Day 6, 8, 10, 11, 14 and 15 after a single dose of 34 Gy or on Day 8, 10, 12, 14, 15 and 18 after a total dose of 46 Gy, given as 3 fractions in an overall time of 6 days. Three animals were used at each of these time points. The oesophagus and the rest of the upper alimentary tract was excised, fixed in 10% neutral buffered formaline and stained with haematoxylin and eosin.

Irradiations

X-rays were generated in a Pantak set operating at 240 kVp and 15 mA, filtered with 0.25 mm Cu and 1.0 mm Al [half-value layer (HVL) = 1.3 mm Cu]. The dose rate was 1.8 Gy min^{-1} . Four unanaesthetized mice were irradiated at a time under air breathing conditions; the dose uniformity at the four positions was within $\pm 2\%$. Basic dosimetry was performed with a Farmer-Baldwin ionization chamber and *in vivo* checks were carried out with TLD dosimeters. The animals were restrained in a 25 mm diameter Perspex tube, with supports under each axillae that held the rib cage gently but firmly in a central position. The body of each mouse was shielded with a 9 mm lead insert, except in the thoracic area in which the lead thickness was 3 mm, allowing a small rectangular cut-out for the mediastinal field. The oesophagus was irradiated with an anterior-posterior field, 17 mm long by 7 mm wide, which included the mediastinum and only the central parts of the lung. The estimated variation from the mid-line position was $\leq 5\%$. The tight pattern of response for single doses for four individual mice (Fig. 1a) and those for the fractionated treatments (data not shown) and the small errors shown in Fig. 1b for 8F/15 days, indicate that the irradiation set-up was highly reproducible. The field was defined and checked by diagnostic X-rays on sample mice before and during the experiment.

Experimental design

Different radiation schedules were used in the same concurrent experiment. Single doses, 4 fractions in either 4 or 13 days, 8 fractions in 8 or 15 days and 12 fractions in 12 or 15 days were given (Table I). Sham-irradiated controls for all the regimes were also included. Non-irradiated controls (eight mice for each radiation schedule) were jugged and taken into the irradiation room for a similar length of time as the corresponding irradiated groups.

Results

The normal oesophagus is lined with a squamous epithelium with a basal layer, maturing keratinized cells and a superficial keratin layer. A submucosa and two muscle layers surround the mucosa and there is an absence of serosa. After a single dose of 34 Gy the histopathological changes observed were as follows.

Day 6. Epithelial cells showed vacuolization and loss

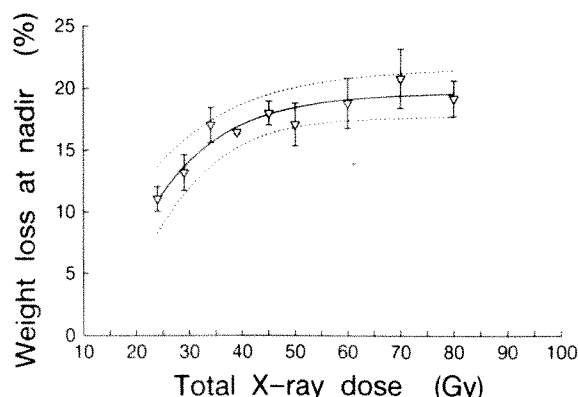


Figure 2. Dose-response curves for the mean nadir of weight loss expressed as percentage of the initial weight (± 1 SEM) after single doses to the mediastinal region of unanaesthetized mice. The dotted lines are the 95% confidence limits.

of cytoplasmic basophilia; spotty areas of destroyed epithelium were observed. Basal cells presented enlarged and sometimes fading nuclei. Subepithelial tissue and the muscularis propria showed intense signs of acute inflammation.

Days 8 and 10. Extensive degeneration of the epithelium with nearly complete cell destruction and areas of denudation were observed. Single basal cells had enlarged and irregular nuclei. Extensive acute inflammation of the subepithelial tissue and of the muscularis propria, with prominent submucosal oedema, was seen.

Day 11. The epithelium, six to eight layers thick, showed signs of parakeratosis and hyperkeratosis. Hyperplasia of the basal cell layer was evident, and cells had enlarged nuclei and prominent nucleoli; an increased mitotic activity was observed (maximal 2 mitosis/HPF (high power field); $\times 400$). There were decreasing signs of acute inflammation in the oesophageal wall.

Days 14 and 15. Eight to 10 epithelial cell layers were observed. Complete re-epithelialization of the mucosa, with hyperkeratosis and parakeratosis, had occurred. Hyperplasia of the basal cells was decreased as well as the mitotic activity (1 mitosis/HPF; $\times 400$). There were no signs of acute inflammation.

With the 3F/6 day regime the changes were similar to those described above, but were seen at a slightly later time. The observations described above on Days 6 and 8 for $1 \times 34 \text{ Gy}$, were seen after 3F/6 days on Days 8–12. Those described for Day 11 were present now on Day 14; those on Day 14 were evident on Days 15–18. However, with the fractionated regime hyperplasia was still prominent 18 days after the first X-ray dose.

Figure 1 illustrates the change in body weight with time for a group of mice receiving local mediastinal irradiation as a single dose of 34 Gy (Fig. 1a). The nadir weight for the four mice in this group occurred 11 days after irradiation and was followed by a progressive increase in body weight. The shaded area represents the mean weight (± 1 SEM) of sham-irradiated controls

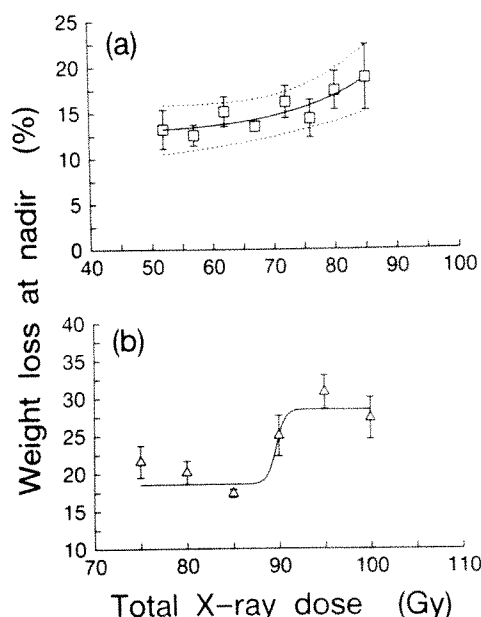


Figure 3. Dose-response curves ($\pm 95\%$ confidence limits, dotted lines) for mean weight at nadir (± 1 SEM) for 4 fractions in 4 days (a) and 8 fractions in 8 days (b).

(eight mice) over the same period of time. After an initial and small decrease in body weight, control animals showed a progressive increase in weight. Figure 1b shows the average weight (± 1 SEM) for mice treated with three different doses of radiation (four animals per dose group) given as 8 fractions in 15 days. For the two lower radiation doses in 8 fractions (65 and 70 Gy), the nadir of weight loss was observed between Days 18–20 after the first radiation dose and at a slightly longer time after treatment for the higher radiation dose (75 Gy). The rate of weight loss for 8F/15 days (Fig. 1b) and for all other schedules was independent of the dose, but the extent of weight loss and the time of onset of recovery was dose-related. This pattern of response is similar to that seen for acute skin reactions and other hierarchically-structured acutely-responding normal tissues (Wheldon & Michalowski, 1986). Control mice, sham-irradiated eight times over a period of 15 days (shaded area, mean ± 1 SEM of eight mice) presented a nadir of weight loss on Day 8 and subsequently a progressive increase in weight.

The response to X-ray single doses, using nadir of weight loss as the method of analysis, is shown in Fig. 2. A dose-dependent increase in weight loss was observed but only up to a 17% level of effect. Above 34 Gy the curve flattened and even with an enormous single dose of 80 Gy a maximum weight loss of not more than 21% was reached. This shape of dose-response curve demonstrates a saturation effect and a remarkable degree of radioresistance for early oesophageal damage. With these data, quantal analysis was not possible since even in the highest dose group the weight of the mice never

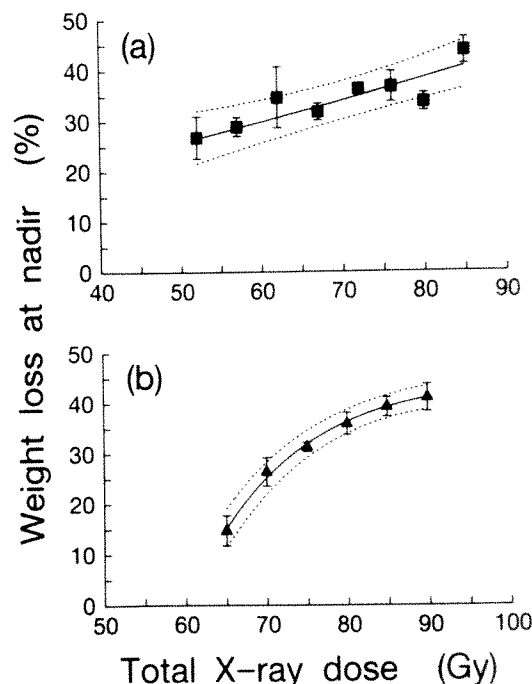


Figure 4. Dose-response curves for mean weight at nadir (± 1 SEM) for 4F/13 days (a) and 8F/15 days (b). The dotted lines are the 95% confidence limits.

reached the “threshold” response level of 26% weight loss of sham-irradiated controls (this value represents the mean nadir weight for all the animals that were treated expressed relative to control animals).

Similar dose-response curves to that for single doses were obtained for 4 fractions given in an overall time of 4 days and 8 fractions in 8 days (Fig. 3). By contrast to the single dose data, with the 4F/4 days regime (a) there was a slight increase in effect in the higher dose groups and an increase in the absolute level of weight loss for 8F/8 days [31% of the initial weight for 8×11.9 Gy; (b)].

Figure 4 shows that extending the overall time can increase the steepness of the dose-effect curve. Figure 4 (a) illustrates data for 4F given in 13 days and in (b) data for 8F/15 days. Higher levels of effect could be achieved when the irradiation was extended from 4 to 13 days for the first regime and from 8 to 15 days for the second schedule (cf. Fig. 3). The increase in sensitivity could be a result of reoxygenation occurring with the longer treatment times and/or of distribution of cells into more sensitive phases of the cell cycle.

The percentage of mice whose weight was 26% or less of sham-irradiated controls after the end of an irradiation schedule is shown in Fig. 5, as a function of dose for 4F/13 days (a), 8F in 8 days (b) or 15 days (c). For comparison, data for 12F/15 days, obtained concurrently with these other fractionated regimes, has been reproduced from Marino et al (1990). Using this quantal

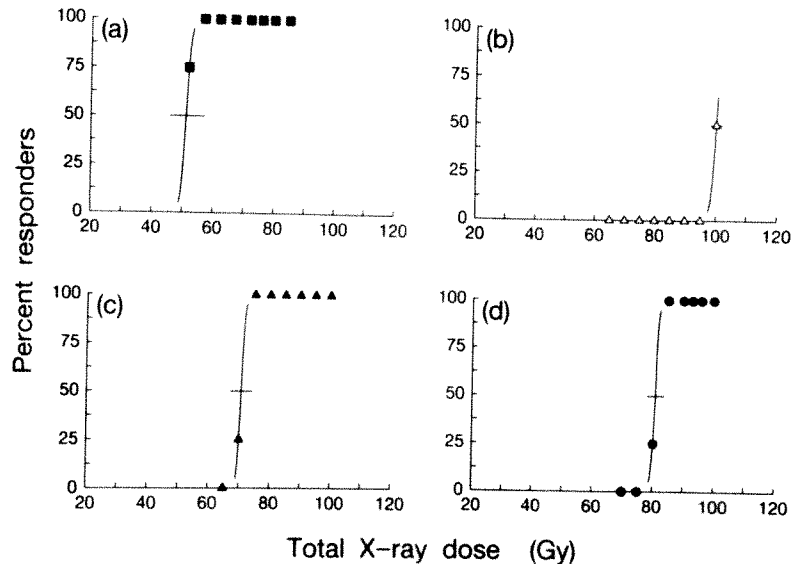


Figure 5. Percentage of mice whose weight loss after the end of treatment was $\geq 26\%$ of sham-irradiated controls, for 4F/13 days (a), 8 fractions in 8 days (b) and 8 fractions in 15 days (c). In (d) data for 12F/15 days, redrawn from Marino et al (1990), are presented for comparison. Errors are 95% confidence limits.

method, steeper dose-effect curves were obtained for all these schedules than for nadir of weight loss and, although the number of mice per dose point was small, the errors ($\pm 95\%$ confidence limits) were not large. The dose range over which a dose-effect relationship was observed was narrow; however, this quantal end-point was a useful method for assessing acute oesophageal damage. Quantal responses for mice weighing 25, 27 and 28% of controls were also calculated (data not shown). α/β ratios obtained using the direct analysis (Thames et al, 1986) were not significantly different for these four levels of response.

From the nadir of weight loss, isoeffect doses were obtained and α/β ratios were then derived using non-linear least squares regression as proposed by Tucker (1984), with weighting of $(1/(95\% \text{ CL})^2)$. The α/β ratios for nadir of weight loss, for both the long (isoeffect level of 30%) and the shorter overall time (16–20% level), were similar and characteristic of an acutely responding normal tissue (11–17 Gy). α/β values were also calculated for other published data using a similar procedure. The direct analysis method, for the quantal response level of 26% (Fig. 5), gave a smaller α/β than those

obtained for the nadir of weight loss. However, the 95% confidence limits on all the values are large, and the difference between them was not statistically significant. No quantal analysis was possible for the single dose or the 4F/4 days regime, since no mice in the former, and only a few in the latter, reached the threshold value of 26%. Table II summarizes the α/β ratios.

Discussion

The histopathological changes observed in the oesophagus of unanaesthetized mice, after a single dose of 34 Gy, using a small mediastinal field, were similar to those reported previously for rats (Jennings & Arden, 1960; Kurohara & Casarett, 1972) and mice (Phillips & Margolis, 1972; Phillips & Ross, 1974) after whole thorax irradiation. It is of interest that the nadir of weight loss occurred on Day 11 (Fig. 1a), the time at which evidence of epithelial regeneration was observed histologically. Comparable changes were observed for a regime of 3 fractions in 6 days to a total dose of 46 Gy, but, as expected, the changes occurred 2–3 days later than after single doses. Irradiation of the oesophagus

Table II. α/β ratios ($\pm 95\%$ confidence limits) for mouse oesophagus for weight loss or lethality

Assay	Level of effect	α/β (Gy)	Number of fractions	Overall time (days)	Reference
Weight loss†	16–20%	11.4 ± 15.0	1,4,8	1,4,8	This paper
	30%	17.4 ± 7.9	12,12,8,4	12,15,15,13	This paper
	LD ₅₀	18.2 ± 8.5	1,2,10	1,14,11	Phillips & Ross (1974)
Lethality†	LD ₅₀	16.6	1,2,5,10	1,2,5,12	Hornsey & Field (1979)
	26%	7.3 ± 5.5	12,12,8,4	12,15,15,13	This paper

†Calculated using non-linear least squares regression (Tucker, 1984).

‡Calculated using the direct analysis method (Thames et al, 1986).

leads to death of the basal epithelial layer (thus preventing the replacement of the rapidly maturing squamous cells), degeneration and denudation of the epithelial layers and intensive submucosal inflammation. Areas of degeneration are seen to co-exist with areas of regeneration and the structural changes correlate well with the gross observations of decreased food intake, body weight loss and animal lethality (Kurohara & Casarett, 1972; Phillips & Ross, 1974; Marino et al, 1990; this paper). By contrast, Michalowski and Burgin (1982) have suggested that duodenal ulcers, induced as an abscopal effect after whole or partial thoracic irradiation, would be the mechanism of death in mice. In our studies, although body weight loss and not lethality was chosen as the end-point, some animals died or were sacrificed because of an unacceptable general condition. These deaths occurred over a similar period of time to that reported by Kurohara and Casarett (1972) and Phillips and Ross (1974) and we observed no evidence of gastric or duodenal ulcers.

The oesophagus is a dose-limiting organ in both conventional, radical and non-conventional (e.g. accelerated radiotherapy) clinical radiotherapy. The acute oesophageal syndrome seen in rodents may be similar to that seen in patients receiving thoracic irradiation in whom marked dysphagia and decreased food intake is observed (Seaman & Ackerman, 1957; Phillips & Margolis, 1972; Fajardo, 1982; Saunders et al, 1989). There is a need for a non-terminal end-point with which to assess the time-dose-fractionation parameters of the oesophageal mucosa. Although lethality at 4 weeks after whole thorax irradiation has been used as an end-point for acute oesophageal damage (Phillips & Ross, 1974; Hornsey & Field, 1979), death due to starvation and dehydration is a terminal, non-humane and clinically non-desirable assay. By contrast, weight loss is a non-invasive, sequential and easily applicable assay, and, as shown here and in a previous publication (Marino et al, 1990), it can give good dose-response relationships. It may be that reduced food intake and/or body weight loss show a similar dose-effect relationship in patients as seen in rodents (Kurohara & Casarett, 1972; Marino et al, 1990; this publication).

Sensitivity to dose fractionation

The single dose and fractionated data for the shorter overall time (Figs 2 and 3) all show a marked degree of radioresistance suggesting that, under air-breathing conditions, the rodent oesophagus is appreciably hypoxic. The large dose-modifying factors reported for single-dose studies using low oxygen concentration (Phillips & Margolis, 1972) or when administering the chemical radiosensitizer, misonidazole (Hornsey & Field, 1979), are evidence of oesophageal hypoxia as are the big D_2-D_1 values obtained for this tissue (Carsten & Noonan, 1964; Phillips & Ross, 1974; Hornsey & Field, 1979). Furthermore, we have observed marked radiosensitization with misonidazole in single and fractionated X-ray treatments as well as high relative biological effectiveness values (Hirn-Stadler, unpublished data).

Thus a uniform degree of hypoxia may exist in the oesophageal mucosa of the mouse, similar to that reported for rodent epidermis (Hendry, 1979; Stewart et al, 1982). Results presented here suggest that hypoxia is present even after smaller doses per fraction (Fig. 2 cf. Fig. 3) and by extending the overall treatment time to 12 days or more, the steepness of the dose-effect curves and the absolute sensitivity were increased (Fig. 3 cf. Fig. 4), indicating perhaps that reoxygenation is more effective with these longer overall times and/or that there is reassortment of cells into more sensitive phases of the cell cycle.

The values of α/β obtained for nadir of weight loss and for quantal response are in agreement with values obtained with the $LD_{50/28d}$ end-point after whole thorax irradiation in anaesthetized mice (Phillips & Ross, 1974; Hornsey & Field, 1979), or for weight loss after localized mediastinal irradiation in non-anaesthetized animals (Hirn-Stadler et al, unpublished data). The α/β ratios, an indirect measure of fractionation sensitivity, obtained for acute oesophagitis are in general higher than those reported for most other acutely responding normal tissues and are also consistent with the existence of a uniform degree of hypoxia (for summary, see Thames & Hendry, 1987).

In the study of Hornsey and Field (1979), the overall time varied from 2 to 12 days for the different fractionated regimes; nevertheless the α/β (~ 16 Gy) was similar to those derived from data where far smaller variations in overall time have been used (Phillips & Ross, 1974; Hirn-Stadler et al, unpublished data; this paper). This suggests that there is little or no compensatory proliferation during a 12-day treatment period, although cellular regeneration can commence as early as 7 days after irradiation (Phillips & Margolis, 1972). Similarly, no evidence of radiation-induced proliferation was reported in mouse skin using small doses per fraction and overall times as long as 16 days (Tsang et al, 1991). However, this observation could actually reflect a balance between proliferation and self-sensitization resulting from reoxygenation and/or reassortment.

Conclusions

To our knowledge, the only assay used to assess radiation damage to the oesophagus has been animal lethality after whole thorax irradiation. This paper shows that changes in body weight after single doses, but especially fractionated treatments, can be used as an end-point for acute oesophagitis. Furthermore, a technique has been developed that allows the mediastinum of unanaesthetized mice to be irradiated, without irradiating the whole of the thorax. These quantitative changes correlated well with the qualitative histopathological changes observed either after a single dose of radiation or with a 3F/6 day regime. The α/β values indicate that the acute oesophageal reaction in rodents, like other acutely reacting normal tissues, will not be spared by hyperfractionation. The shapes of the dose-response curves seen with both single doses and 4F/4 day and 8F/8 day and the large α/β ratios suggest

that this organ is under a considerable degree of hypoxia even when smaller, fractionated doses of radiation are used.

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Technical note

Development of video frame store and distortion correction facilities for an external-beam radiotherapy treatment simulator

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During the simulation of an external-beam X-ray radiotherapy treatment, a low-energy X-ray source (tube voltage ≈ 50 –100 kVp) is used to irradiate the patient and the transmitted intensities are recorded either by X-ray film or an X-ray image intensifier (XRII). The XRII enables the clinician to observe immediately the result of moving the patient within the X-ray beam in order to select an appropriate treatment field. Since the image is produced by the XRII in real time, the image is lost from the screen whenever the X-ray screening button is released. Therefore, the screening button is normally kept depressed during the time in which the clinician reaches a decision about the size and position of the correct treatment field. Since the displayed image is not altered during the decision period, a higher than necessary dose is delivered to the patient, and also to the clinical staff present, during the simulation session.

To reduce this dose and simplify the simulation procedure, a device has been constructed which maintains the image on the television monitors in the simulator area whenever the screening button is released. This enables the clinician to view the most recent XRII simulation image during any decision period without delivering any further X-radiation to the patient. The true XRII image is displayed as soon as the screening button is next depressed. This mode of operation is termed the "active hold" mode. The device, consisting of a video frame store and IBM-PC, has been in use in our department for over a year and has become an integral part of the simulation procedure.

As part of a continuing programme of research into conformal therapy in our centre, we have developed two digital imaging devices for use at treatment time, one of which produces digital portal images using the treatment beam (Morton, 1988; Morton et al, 1991) and the other which produces computed tomographic (CT) images from a fan beam of treatment-energy X-ray

photons (Lewis et al, (submitted for publication)). The images obtained from these devices may be used to study the reproducibility of set-up between each fraction of a patient's treatment since both detection systems may be rigidly attached to the rotating gantry of the linear accelerator. To form an accurate analysis of set-up variation, it is necessary to compare the treatment-time image with a particular reference image, which we normally choose to be the corresponding simulation (or diagnostic CT) image. In the case of portal images, the output from the simulator's XRII may be digitized and stored to disk such that a true digital comparison of the simulation and treatment-time images may be made.

System design

The device consists of a Colorado Video frame store (model 492 Video Subtractor) connected to a standard IBM-PC via a parallel interface supplied with the video frame store (Fig. 1). The digitized image is stored with 512×512 pixel elements to an accuracy of 8 bits. The frame store is controlled by a program written in "C". The program displays a single menu, which allows the operator to select either normal simulator video operation or the "active hold" mode described above. Further menu options control the storage and recall of images from floppy disk.

The computer is connected to the simulator screening switch via the parallel printer interface of the PC. Since the parallel printer interface is a standard part of an IBM-PC, this removes the need to purchase extra interface cards. To reduce the possibility of electrical interference between the simulator and computer, a spare set of contacts on the screening button foot-switch is used to control the computer. The switch is adjusted such that the set of contacts connected to the computer change state momentarily before the main contacts when the screening button is released.

When the video system is operating in the active hold mode, the computer first checks the status of the simulator screening foot-switch. If the switch is depressed (*i.e.* the X rays are on) the frame store memory is released and the current video image is stored. This takes about 30 milliseconds to complete and repeats until the foot-switch status changes. When the foot-

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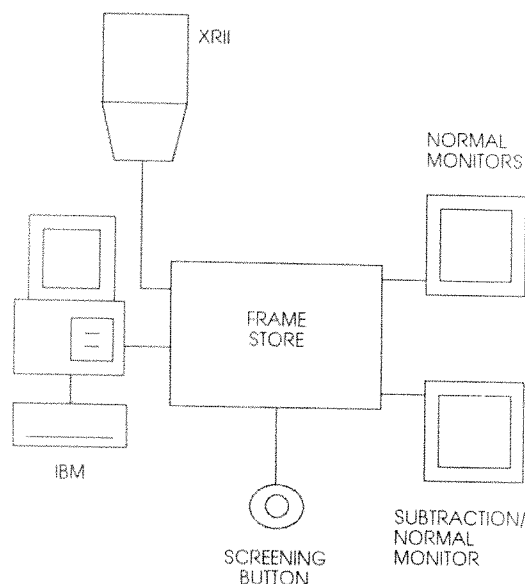


Figure 1. A block diagram of the simulator video attachment. The IBM-PC is connected to the frame store via a parallel interface. The foot-switch screening button is connected between the "out of paper" connection on the parallel printer interface and ground.

switch has been released, the contents of the frame store memory are not released and the image remains on the screen. Therefore, the most recent "beam on" image is maintained on the video monitors.

The contents of the frame store memory may be written to a floppy disk at any time for archive purposes or comparison with treatment-time images as described above. Since the storage capacity of a standard IBM format floppy disk is only 360 kB, a 512×512 pixel image virtually fills a complete disk. To save on disk storage space, each image is condensed to a size of 256×256 pixels before storage. This size reduction is accomplished by storing only the odd-numbered row and column intensities to disk. The information contained in the even-numbered rows and columns is discarded. Although this method is wasteful of the X-radiation that interacts with the XR11, image storage is quick since only 25% of the total 512×512 image pixel values must be transferred from the framestore to the PC prior to storage. The framestore to PC routines are written in assembler. In this condensed form, a complete set of simulation images for a single patient can normally be stored on a single disk. Comparison of the compressed image with the original image revealed no degradation of image quality associated with the compression procedure.

When a condensed image is read back into the frame store, and so displayed on the simulator video screens, each stored pixel intensity is read back into a block of four pixels in the frame store memory. No interpolation or other image processing methods have been implemented since these slow down image recall time.

Currently, an image may be recalled from disk in around 5 seconds using an assembly language subroutine.

Image calibration

X-ray image intensifiers suffer from pin-cushion distortion. This effect can lead to apparent displacement errors in the image of several millimetres relative to the true position in the object. However, patient set-up errors may be of this magnitude (Marks et al, 1974). Thus, since we are interested in forming comparisons between the two image types to an accuracy of around a millimetre, we need to apply a spatial correction method to the digitized simulation image. Two techniques have been developed to facilitate the implementation of such corrections.

First technique

The first method requires, as input, a series of open-field images with the field delineation wires positioned to define a range of square fields of several different, known sizes. For this method it is important that the centre of the field corresponds closely to the centre of distortion. These images are analysed in order to determine the distortion as a function of field position, so that digital resampling of the image may be performed.

Aspect ratio correction. A primary goal of developing this frame store facility has been to obtain digital simulator images for comparison with megavoltage verification images obtained at the time of treatment using a digital scanning system (Morton et al, 1991). The megavoltage imaging system uses a LEXIDATA 3703 image display system, which has a square pixel format. However, the video monitor of the simulator system is of TV format with a pixel aspect ratio of 4 : 3. Hence, all simulator images used on the megavoltage imaging system have digital resampling performed on them to correct for the difference in aspect ratio using standard linear interpolation.

Pin-cushion distortion removal. In Fig. 2 we illustrate the appearance of the field delineation wires of the simulator if pin-cushion distortion is present. The dashed lines indicate the apparent position of the field-defining wires in the uncorrected image; the solid lines represent the true wire positions after distortion removal. It is important that the true positioning of the wires (denoted by the solid lines) be accurately known.

The amount of pin-cushion distortion at a point depends on that point's distance from the centre of the distortion—referred to here as the origin. The distortion is zero at the origin and increases with distance, acting in a line joining that point with the origin.

One may estimate the origin, (denoted by *O* in Fig. 2) as the centre of the circular field of view of the simulator image. Once the origin of the image is known, a co-ordinate system may be constructed. This may then be used to measure the distance of known points from the origin.

Consider the point whose position in the undistorted image is *P* in Fig. 2. We need to calculate its position in

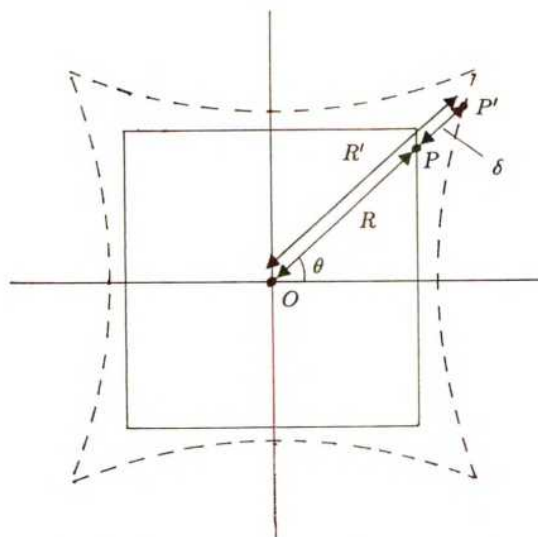


Figure 2. Illustration of the appearance of the field delineation wires if pin-cushion distortion is present. The field crosswires are indicated. The true position of the field delineation wires is shown by the solid square. The dashed line shows their position in the distorted image. The point O indicates the origin about which the distortion occurs. A point P is distorted by the amount δ and appears at P' in the image. R is the distance OP and R' is the distance OP' .

the distorted image, P' . The amount of pin-cushion distortion, δ , is adequately represented by an even function of the point's distance from the origin, OP (odd terms would change sign on reflection about the origin and thus would not give a distortion value purely dependent on distance from the origin as required). A simple Taylor expansion may be used for δ , viz:

$$\delta = \alpha R^2 + \beta R^4 \dots \quad (1)$$

where R is the distance OP and α, β are coefficients. If its distance from the origin of the distorted image, OP' , is measured to be R' , then:

$$R' = R + \delta \quad (2)$$

Since the distortion acts in the direction OP , we may resolve the x and y components of Equation (2) to yield:

$$\begin{aligned} x' &= x + \delta \cos \theta \\ y' &= y + \delta \sin \theta \end{aligned} \quad (3)$$

where the primed quantities are the components of R' and the unprimed quantities relate to R . Thus, once α and β are known, we may take any pixel in a distortion-corrected, output image and calculate the position of the corresponding pixel in the distorted, input image. In general the corresponding pixel will be found to be at a non-integer co-ordinate. Bilinear interpolation may then be used to weight the contribution to the output pixel intensity from the four nearest pixels. In practice, initial

values for α and β are estimated and adjusted until the wires in the open-field images appear undistorted.

Thus, in summary, a functional form for the distortion is established (Equation 1) and the distortion removed from the image using digital resampling, where the x and y transformations are given by Equation 3.

Final corrections. Once the aspect ratio and pin-cushion distortion corrections described above have been implemented, the open-field images obtained contain no distortion and are square in aspect. As discussed in the introduction, these simulator images are compared with images obtained with our megavoltage imaging system (Morton et al, 1991). In order to facilitate this, the simulator images are linearly resampled in the x and y directions once more, so that the pixel size is equal to that of the megavoltage images. The orientation of the central crosswires is then measured to determine the simulator image rotation. This is then set to zero degrees by further resampling.

Evaluation. The in-house software developed to implement this whole procedure requires 1 minute of CPU time on our microVAX II computer. In Fig. 3 we illustrate the effects of each stage of the image calibration procedure. In order to evaluate the final residual distortion, a test phantom was constructed and imaged. This phantom consists of a square array of 2 mm diameter holes, separated by 2 cm, drilled into a thin copper plate. The apparent positioning of the holes, after distortion correction, was compared with their true positioning, established by measurement of the plate.

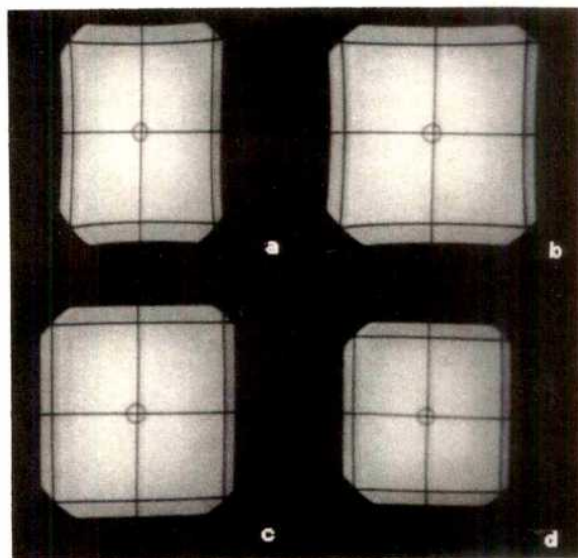
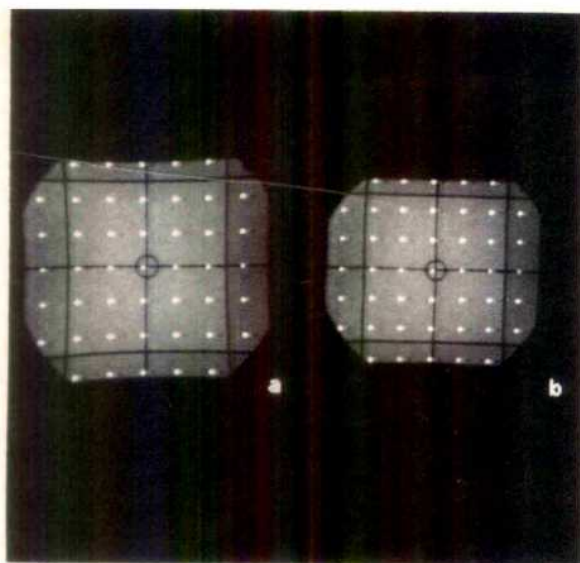


Figure 3. Illustration of the effects of each stage of the first distortion removal procedure: (a) shows the original image; (b) shows the image after aspect ratio correction; (c) is the image after pin-cushion distortion has been removed, and in (d) the final correction procedures have been applied. To produce image (c) the values $\alpha = 6 \times 10^{-4}$ pixels⁻², $\beta = 4 \times 10^{-8}$ pixels⁻⁴ were used in Equation (1).



The results revealed a maximum error of 1.5 mm, with an RMS deviation of less than 0.2 mm over the whole field. The main contribution to this value comes from those points at the field edge: the RMS error was less than 0.1 mm for the central 50% of the field. Thus, the residual distortion was found to be greatest at the edge of the field. These distortion figures should be compared with the distortion measured for the uncorrected image of the test phantom, where an RMS value of 0.65 mm (with a maximum distortion of 9 mm) was found for the holes.

Second technique

The second method uses, as input, the image of the test phantom described above. Initially, as for the first technique, digital resampling was performed to correct the pixel aspect ratio. Having achieved this, the resulting image [Fig. 4(a)] was viewed. The position of each hole in the image was taken as a grid point. Each grid point was compared with its expected position for zero distortion. Such a comparison provided values for the error in the x and y directions at the grid points.

To calculate the distortion correction at other points, the method of bilinear interpolation was used. For those pixels enclosed by four grid points, the correction was obtained by interpolating from the four nearest grid points. For pixels in the corner regions, the distortion correction was simply taken to be that of the nearest

grid point, and for edge regions it was calculated by interpolating from the two nearest grid points.

Evaluation. The result of this point-by-point mapping procedure is shown in Fig. 4(b). By applying this method to several images of the same test phantom, but at different magnifications, the accuracy could be determined. These results indicate an RMS error of less than 0.1 mm, with a maximum error, for any grid point, of 1.5 mm. The RMS error across the image was found to be uniform in size. This method requires 40 seconds of CPU time on our microVAX II computer.

Conclusion

A simple and reliable system has been developed to provide some of the facilities available from much more expensive commercial video systems designed for use with a simulator. Furthermore, permanent archive facilities have been provided such that simulation images may be both reviewed at a later date and also used as reference images in a digital, treatment-time, portal imaging system. By maintaining the simulation image on the video screen after the screening button has been released, X-ray dose to both the patient and staff may be reduced.

To enable the digitized simulation images to be used as reference images for determining set-up error during external-beam radiotherapy, it is necessary first to remove all spatial distortion from the images. This is accomplished by the method of digital resampling.

Acknowledgments

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Case reports

An unusual cause of a pain in the calf

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Keywords: Calf, Venous, Haemangioma

Calf pain is a common cause for a request for a venogram to exclude the possibility of a deep venous thrombosis. An unusual cause of calf pain due to a venous haemangioma is presented and the radiological features are reviewed.

Case report

A 42-year-old Caucasian woman attended the Accident and Emergency Department with a 2-day history of increasing right-sided calf pain. As a child, she had been told she had an abnormality in her right calf that was inoperable. The venogram and computed tomographic (CT) scan of the calf are shown in Figs 1 and 2.

Discussion

The venogram shows normal deep vein anatomy but an abnormal collection of dilated tortuous disorganized

veins in the calf communicating with the deep venous system is seen. No arterio-venous communication was demonstrated.

The CT scan of the calf in the same patient performed with vascular enhancement showed the venous haemangioma to be within the calf muscles. Clinical examination of the limb revealed a further small subcutaneous haemangioma over the right buttock with no evidence of limb hypertrophy.

Venous haemangioma of the calf is an unusual cause of calf pain. Venous haemangiomas are formed from venular capillaries or large veins. In the former case they form the so-called port-wine stain, which are cutaneous and often multiple. Malformations of the larger veins may affect the upper or lower limbs but are usually solitary (Browse et al, 1988). They may occur in association with other abnormalities, e.g. prominent superficial

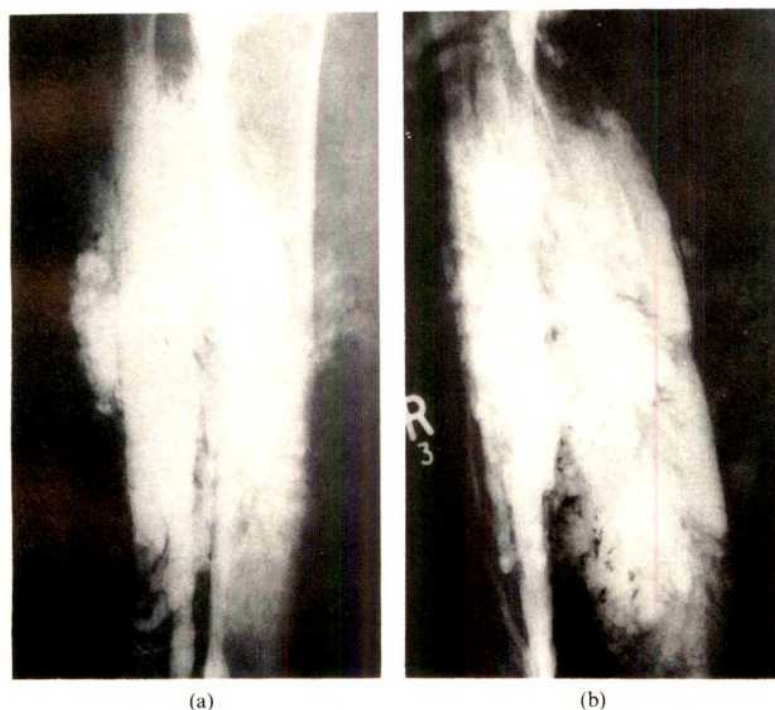


Figure 1. (a, b) Venograms of the right calf.

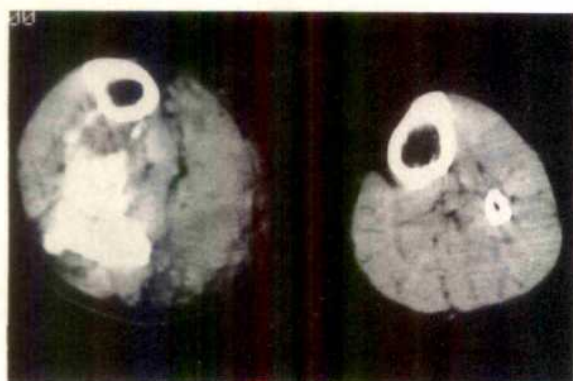


Figure 2. Computed tomographic scan of both calves (the right calf performed with contrast medium injected in the right foot).

veins, hemihypertrophy of the limb and deep venous hypoplasia as the Klippel-Trenaunay syndrome (Klippel & Trenaunay, 1900). In our case, the patient's calf pain was due to a solitary deep intramuscular venous haemangioma in the calf.

A venous haemangioma is essentially a collection of large dilated disorganized veins that communicate with the normal venous system. They are benign, but may fluctuate in size. Thrombosis and thrombophlebitis are common complications. The arterial system is normal in these patients but there may be associated lymphatic dilatation (Trout et al, 1985).

Clinically, deep venous haemangioma usually presents with pain, which is described as a dull ache present all the time, relieved by elevation of the limb.

Exacerbation of the pain may be due to episodes of haemorrhage, thrombosis or thrombophlebitis.

Useful radiological investigations include a plain radiograph of the calf, which may show soft-tissue swelling, phleboliths and, occasionally, translucent areas in the bone if there are dilated veins within it. A Doppler probe may be useful to exclude arterio-venous malformations (Van Der Molen, 1976). An ascending phlebogram will show dilated tortuous venous channels communicating with a normal deep venous system. Occasionally it may be difficult to demonstrate the haemangioma by venography. A CT scan with injection of contrast medium confirms the haemangioma and shows the relationship between the lesion and the surrounding muscles and joints. This is important to the surgeon as it is easier to remove more superficial haemangiomas and the intermuscular haemangioma whereas the intramuscular lesions are hard to remove without excising all the muscle. Fortunately, symptoms rarely justify this drastic measure (Lofgren & Lofgren, 1985).

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Unusual magnetic resonance findings in Wilson's disease

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Keywords: Wilson's disease, Magnetic resonance imaging

Wilson's disease or hepatolenticular degeneration is an uncommon genetic disorder of copper metabolism, characterized by abnormal deposition of copper especially in the liver and brain. Computed tomography (CT) and magnetic resonance (MR) findings in Wilson's disease have been described (Kendall et al, 1981; Lawler et al, 1983; Aisen et al, 1985). We report unusual MR findings in two cases of Wilson's disease.

Case reports

Case 1

A 28-year-old female presented with tremor and difficulty in speaking and walking for several months. Physical examination

showed Kayser-Fleischer rings, tremor, spasticity, rigidity, dysphasia and dysarthria. Serum caeruloplasmin was low. The patient also had long-standing cirrhosis. Computed tomography of the brain showed symmetrical low-density lesions in the basal ganglia. Magnetic resonance imaging revealed areas of increased signal intensity in the basal ganglia and caudate nuclei in both proton density and T_2 -weighted images. Foci of low signal intensity were seen within the hyperintense basal ganglia (Fig. 1).

Case 2

A 19-year-old male presented with tremor and difficulty in writing for several months. Physical examination showed Kayser-Fleischer rings, tremor and signs of liver cirrhosis.

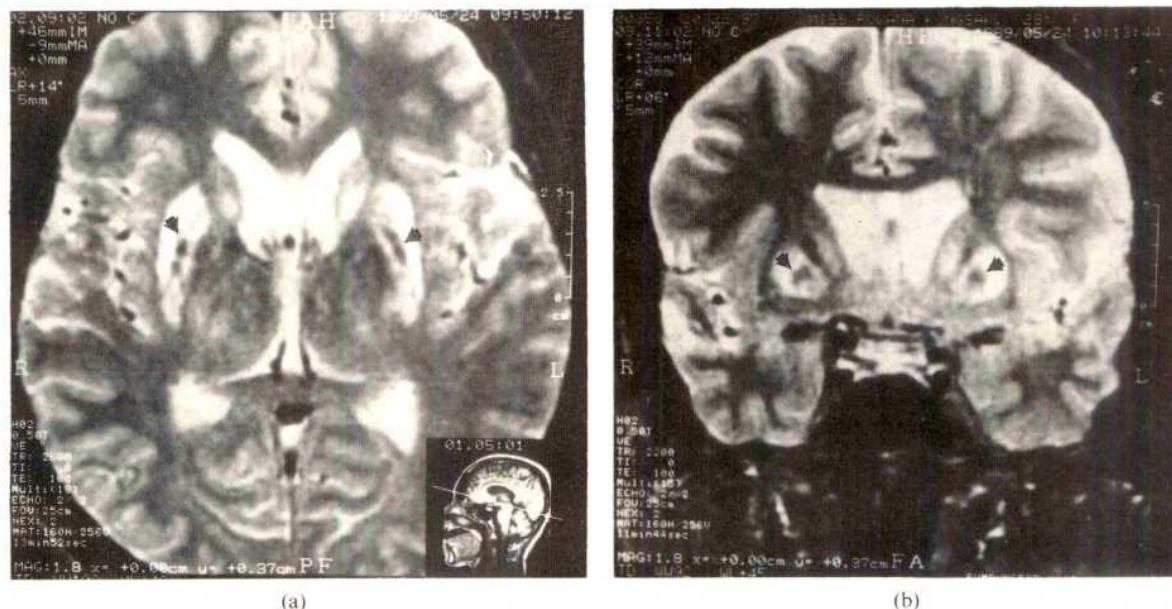


Figure 1. Magnetic resonance of the brain, T_2 -weighted images. (a) Axial view and (b) coronal view show increased signal intensity in basal ganglia and caudate nuclei with low signal intensity foci within the hyperintense basal ganglia (arrows).

Serum caeruloplasmin was low. Computed tomography of the brain showed low-density lesions in both basal ganglia. Magnetic resonance imaging revealed increased signal intensity areas in both basal ganglia and caudate nuclei. Small foci of low signal intensity were also noted in the hyperintense basal ganglia and caudate nuclei (Fig. 2).

Discussion

In Wilson's disease, caeruloplasmin, the serum transport protein for copper, is deficient and copper is

deposited in the brain and liver. In the brain, cavitation and gliosis of the basal ganglia, brain stem and cerebellar nuclei occurs. Findings on CT in Wilson's disease are low-density lesions in the basal ganglia and widespread brain atrophy (Kendall et al, 1981). Magnetic resonance imaging appeared to be more sensitive in demonstrating the lesions and correlated better with clinical symptoms than did CT. The previously described MR findings are increased T_2 signal in lenticular, thalamic, caudate and dentate nuclei as well as the

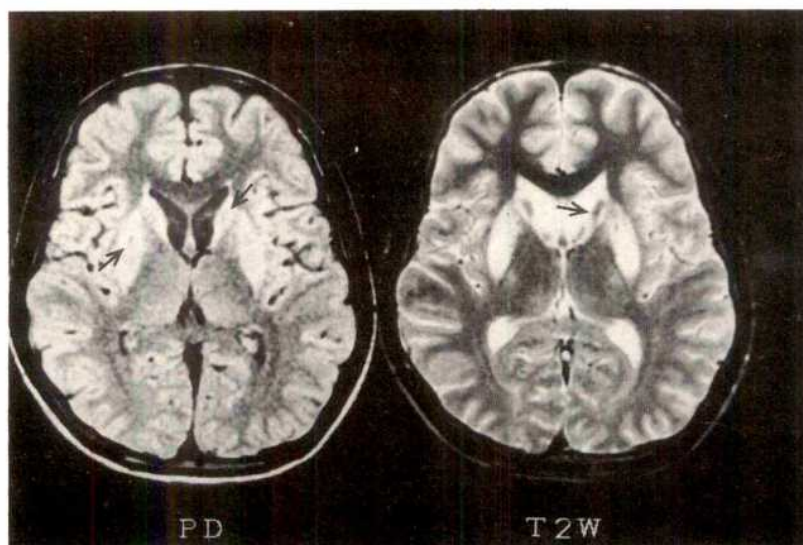


Figure 2. Magnetic resonance of the brain; proton density and T_2 -weighted images show increased signal intensity in basal ganglia and caudate nuclei with low signal intensity foci within the hyperintense area (arrows).

brain stem (Lawler et al, 1983; Aisen et al, 1985). Decreased T_2 signal in Wilson's disease has been mentioned once by Yuh and Flickinger, (1988), who suggested that the decreased signal was due to the paramagnetic effect of copper. Both of our cases show foci of decreased T_2 signal within the hyperintense basal ganglia and in one case also in caudate nuclei. The patients presented with both neurological symptoms and cirrhosis, indicating the long duration of untreated disease. It is possible that the concentration of copper is so high that its paramagnetic T_2 shortening effect outweighs the T_2 increasing effects of surrounding oedema and gliosis resulting in low signal intensity foci. Another possible cause of decreased T_2 signal is iron deposition from previous haemorrhage, which may occur in association with basal ganglion destruction.

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Demonstration on computed tomography of two pseudoaneurysms complicating chronic pancreatitis

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Keywords: Computed tomography, Chronic pancreatitis, Pancreatic pseudoaneurysm, Pancreatic pseudocyst

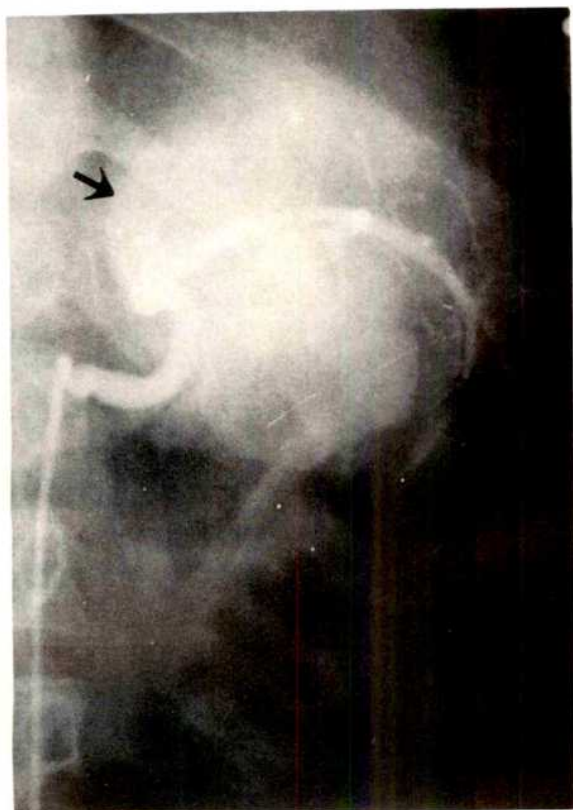
Arterial pseudoaneurysm as a complication of chronic pancreatitis is relatively uncommon. Most radiologists are well aware of pseudocyst and abscess formation, but not of this vascular complication (Burke et al, 1986). In the English language literature, we found reports of only seven cases documented by computed tomography (CT) of pseudoaneurysm occurring secondary to pancreatitis (Borlaza et al, 1979; Foley et al, 1980; Nino-Murcia et al, 1983; Burke et al, 1986; Falkoff et al, 1986). These cases, however, involved only one artery in each patient, namely the splenic, hepatic or gastroduodenal artery. We report here the case of a man with chronic pancreatitis who developed pseudoaneurysms of both the splenic and pancreaticoduodenal arteries. In this first CT-documented report of such a case, we emphasize the role of CT as an accurate, non-invasive diagnostic method for this easily misdiagnosed lesion.

Case report

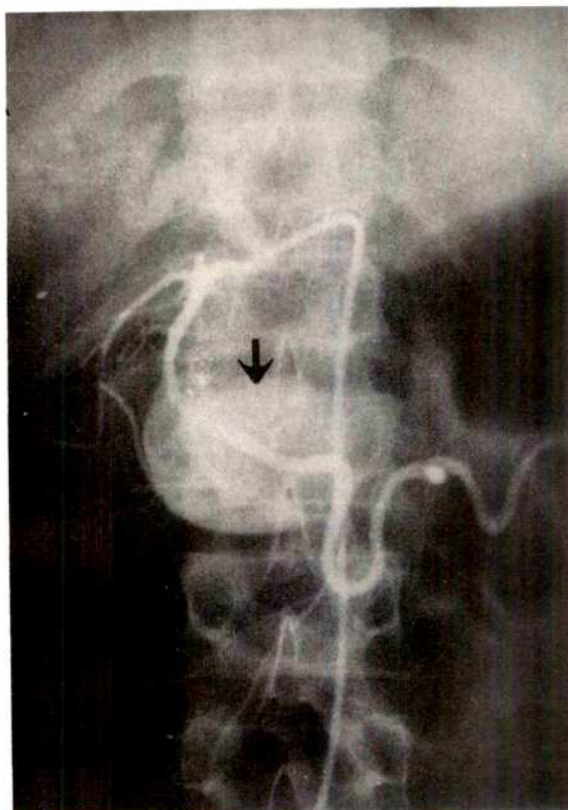
A 32-year-old man, with a history of alcohol abuse for 10 years and intermittent epigastric pain for 1 year, presented at Choburi Provincial Hospital in Thailand with severe abdominal pain, nausea and vomiting. Physical examination revealed an ill defined, right subcostal mass. Ultrasonography (US) showed a homogeneously low-echoic mass with distal acoustic enhancement, about 5 cm in diameter, located at the

head of the pancreas, suggestive of a pancreatic pseudocyst. Evidence of chronic cholecystitis was also demonstrated. The patient later developed high fever and jaundice. Follow-up US, 10 days after the first study, revealed enlargement of the cystic lesion at the pancreatic head to a diameter of about 7.5 cm. The previously homogeneous cystic mass showed mixed echogenicity suggestive of either pancreatic abscess or infected pseudocyst. Exploratory laparotomy was carried out and a cholecystectomy was performed to remove a chronically inflamed gallbladder. The pancreas was found to be sclerosed and nodular, indicative of chronic pancreatitis. A large cyst was seen at the pancreatic head and noted to be adherent to the adjacent structures. Aspiration of the cyst yielded frank pus from the right portion, but fresh blood from the left portion. A Malecot tube was inserted into the pocket of pus for drainage, while the pocket of blood was left undisturbed. The pancreatic tail was not explored. Post-operation, a celiac angiogram was performed and revealed two large aneurysm-like lesions. One, located at the pancreatic tail, was supplied by the pancreatic magna branch of the splenic artery [Fig. 1(a)] while the other, at the pancreatic head, was supplied by the pancreaticoduodenal artery [Fig. 1(b)]. At this point, the patient was referred to Chulalongkorn University Hospital for further management.

At presentation in this hospital, the patient was very pale and toxic. His body temperature was 40°C, pulse rate 120, blood pressure 110/60, and haemoglobin 8.9 gm%. An ill defined mass was palpable in the epigastrium. An emergency



(a)



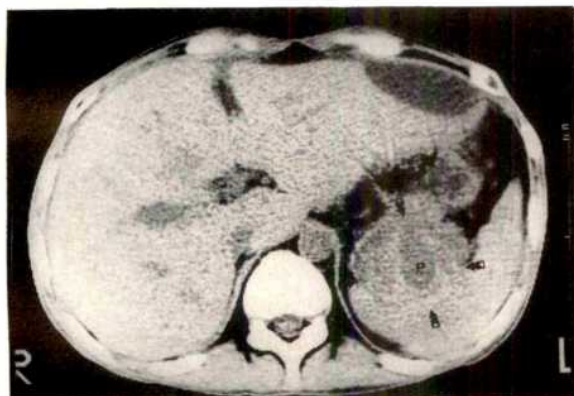
(b)

Figure 1. Celiac angiography revealing two large aneurysm-like lesions. (a) Selective splenic arteriogram shows a lesion (arrow) fed by the pancreatic magna branch of the splenic artery. The splenic artery is stretched and bowed by the aneurysm. (b) Selective gastroduodenal arteriogram shows a lesion (arrow) supplied by the pancreaticoduodenal artery.

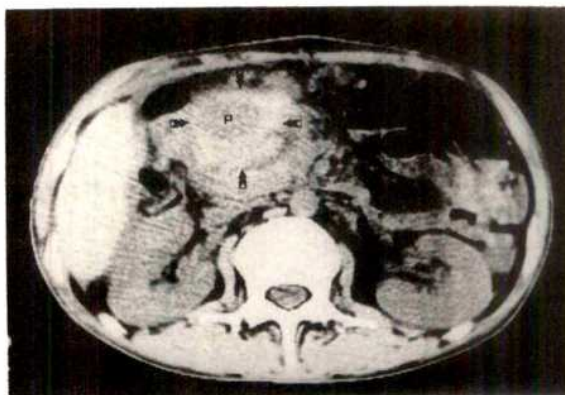
CT scan was performed. The study showed evidence of two large, mixed-density masses at the tail and head of the pancreas. Each mass contained a low-attenuation, cyst-like portion (Fig. 2). After an intravenous bolus injection of iodi-

nated contrast medium, CT demonstrated enhancement within the cystic portion of both masses, strongly suggesting the presence of two pseudoaneurysms (Fig. 3).

A second exploratory laparotomy was performed. Two



(a)



(b)

Figure 2. Plain CT scans disclosing two large, mixed-density masses at the tail and head of the pancreas. (a) A complex mass (arrowheads) at the pancreatic tail with relatively low density (p) in the middle of the mass. (b) A mixed-density mass (arrowheads) at the pancreatic head with relatively low density (p) in the right aspect of the lesion.

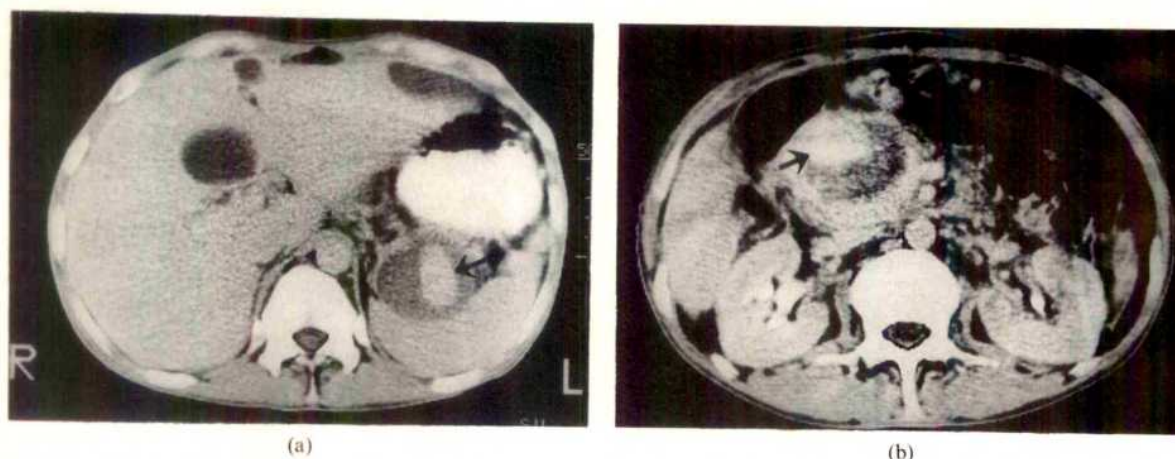


Figure 3. Contrast-enhanced CT scans showing homogeneous enhancement (arrows) within the relatively low-density areas seen in Fig. 2, indicative of the pseudoaneurysms. (a) The lesion at the pancreatic tail. Low-density areas adjacent to the left and right lobes of the liver are collections of fluid within the left subphrenic space and in the gallbladder fossa. (b) The lesion at the pancreatic head.

haemorrhagic cysts, one at the head and one at the tail of the pancreas, were identified. The cyst at the head of the pancreas appeared about to rupture. It was opened and an infected blood clot was removed. A bleeding vessel at the posterior wall of the cyst was ligated, followed by cystojejunostomy and jejunojejunostomy for internal drainage. Distal pancreatectomy with splenectomy was performed to remove the pseudoaneurysm at the tail of the pancreas. The patient recovered after an extended hospital course and was discharged home.

Discussion

Pseudoaneurysms of pancreatic vessels are almost always associated with chronic pancreatitis (White et al, 1976). Erosion of pancreatic and peripancreatic vessels by pancreatic enzymes represents the major factor in the pathogenesis of these lesions (Stanley et al, 1976). In chronic pancreatitis, these same processes commonly result in vascular damage recognized angiographically as microaneurysms and irregularity of parenchymal arteries (Boijesen & Tylan, 1972). Pseudoaneurysms may be considered the most severe manifestation of a spectrum of vascular pathology. A pseudoaneurysm may develop within a pre-existing pancreatic pseudocyst, thus resulting in the conversion of the pseudocyst into a pseudoaneurysm (Vujic, 1989).

The splenic artery is the most frequent site of pseudoaneurysm formation because of its contiguity with the pancreas (Stabile et al, 1983). The association of splenic artery aneurysm and pancreatitis was first recognized at the time of surgery (Lower & Farrell, 1931), and it was another 30 years before Baum et al (1965) illustrated a ruptured splenic artery aneurysm following pancreatitis by selective celiac arteriography. Other commonly involved sources of bleeding are the pancreaticoduodenal and gastroduodenal arteries, while implicated less often are the left gastric, hepatic and small intrapancreatic arteries (Stabile et al, 1983). The case presented here showed pseudoaneurysmal involvement of both the splenic and pancreaticoduodenal arteries.

Rupture of a pancreatic pseudoaneurysm is one of the most life-threatening complications of pancreatitis, and has an estimated mortality rate of about 50% (Cogbill, 1968; Stanley et al, 1976; Stabile et al, 1983; Vujic, 1989). Thus, early detection when rupture can still be prevented is very important. Rupture of a pseudoaneurysm may occur into a pseudocyst, lesser sac, peritoneal cavity or an adjacent hollow viscus, if there is sufficient intracystic pressure. On rare occasions, the vascular mass may rupture into the pancreatic duct, producing "haemosuccus pancreaticus" (Bivins et al, 1978). Presenting clinical features commonly include abdominal pain accompanied by gastrointestinal (GI) haemorrhage and/or anaemia with shock (Cahow et al, 1983). Our reported case presented with anaemia and shock, signs of both chronic and acute blood loss.

Gastrointestinal haemorrhage occurring in patients with chronic pancreatitis secondary to alcohol abuse is usually caused by non-pancreatic pathology, such as peptic ulcer disease, gastritis and oesophageal varices. Therefore, a diagnosis of ruptured pseudoaneurysm as the cause of GI bleeding may be delayed. Realizing this problem, the importance of pre-operative angiography in patients with acute GI bleeding and a history of pancreatitis has been stressed (Boijesen et al, 1969).

At the present time, ultrasonography is usually the first examination performed if a complication of pancreatitis is suspected. Signs suggestive of vascular involvement include rapid enlargement of a cystic pancreatic mass and/or a sudden change of the cystic echogenicity (Vujic, 1989). The latter sign was seen in our case but, unfortunately, the diagnosis remained unsuspected partly due to unawareness of this complication. Contrast-enhanced CT is one of the most useful modalities for diagnosis of vascular involvement in pancreatitis. Homogeneous enhancement within a cystic portion of a pancreatic mass is strongly suggestive of pseudoaneurysm. As shown in this case, CT clearly

Case reports

demonstrated the pseudoaneurysms at both the head and tail of the pancreas, while the lesion at the tail was missed by both US and the first exploratory operation. Although unlikely, it is possible that the pseudoaneurysm at the tail of the pancreas only developed after the first operation. Once a vascular complication of pancreatitis is suspected, based on US or CT, angiography should be performed to identify precisely the site and source of bleeding. Therapeutic angiographic embolization might be done at this same time, if clinically indicated (Vujic et al, 1984).

The case presented here documents the rare occurrence of two separate pseudoaneurysms that resulted from chronic pancreatitis, and illustrates the usefulness of contrast-enhanced CT as a sensitive method for diagnosis of pancreatic pseudoaneurysms.

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Extensive calcification in the breast in chronic renal failure

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(Received November 1990)

Keywords: Breast calcification, Renal failure

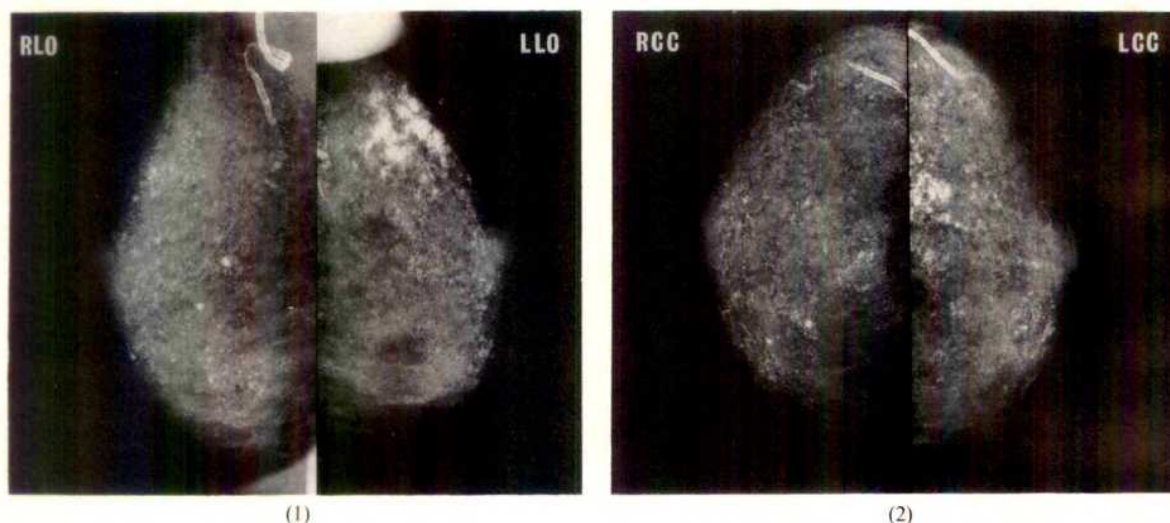
Although soft tissue calcification is a frequent finding in chronic renal failure, extensive calcification in the breast is a very rare feature in this condition. It may present as a non-tender mass or be found incidentally on a chest radiograph or mammogram. We report a case of extensive bilateral breast calcification occurring in a woman with chronic renal failure.

Case report

A 43-year-old female with a long history of chronic renal failure was referred for mammography, having discovered a

lump in her breast on self examination. Renal insufficiency was diagnosed 12 years previously when bilateral staghorn calculi had been removed. Renal transplantation, performed 6 years later, was complicated by multiple post-operative problems including uretero-vesical stenosis and acute rejection. On examination, she had a firm, non-tender mass, 4 × 5 cm in size, in the upper outer quadrant of the left breast.

Mammography showed numerous foci of calcification, densely aggregated and widely scattered throughout both breasts (Figs 1 and 2). These calcifications were particularly aggregated in the upper half of the left breast, lateral to the midline, in an area corresponding to the palpable abnormality.



Figures 1 and 2. Lateral oblique and cranio-caudal mammograms. There is widespread microcalcification in both breasts, particularly aggregated in the upper half of the left, lateral to the midline. Bilateral arterial calcification is also seen.

There was also marked arterial calcification within both breasts. No soft tissue mass or any other stromal abnormality was seen.

Previous radiography had demonstrated extensive changes of renal osteodystrophy and soft tissue calcification, especially vascular and periarticular in situation. Her most recent serum creatine was $1984 \mu\text{mol/l}$ (normal range $60\text{--}110 \mu\text{mol/l}$). No specific treatment was initiated in respect of the mammary mass, which is being kept under observation.

Discussion

Metastatic soft tissue calcification is a well described finding in chronic renal failure. It appears to be related to an increase in serum calcium phosphate product and secondary hyper-parathyroidism (McDougal & Luker, 1977). The commonest sites are the media of arteries, the cornea, periarticular tissues, skin and subcutaneous tissues and multiple visceral organs including the kidney, lung and heart (Parfitt, 1969).

Calcification of the breast parenchyma has been described on only two previous occasions (Sang & Witten, 1977; Cooper & Berman, 1988). In both instances it was an isolated finding, unlike the present case, in which there was widespread evidence of vascular and other soft tissue calcification and renal osteodystrophy.

While vascular calcification in the breast is related to increasing age and diabetes (Leinster & Whitehouse, 1987), other examples have occurred in cases of renal failure (Massry et al, 1969; McDougal & Luker, 1977). In previously reported cases of parenchymal calcification, the calcification, although bilateral, was more localized and of a coarser conglomerate nature than in the current case. As the previously reported cases have been in documented renal failure for only 4 (Sang & Witten, 1977) and 9 months, the extensive distribution

in the present case may reflect the long history of renal failure.

In the case reported by Sang and Witten (1977), the breasts were noted to feel hard on examination, although there were no discrete masses. This case also demonstrated resolution of the calcification following treatment and this has been described previously in calcification in other sites (Johnson et al, 1967; Parfitt, 1969; Meema et al, 1976). Cooper and Berman (1988) reported a presentation similar to the current case of a firm, non-tender mass in the breast.

In neither of the previously reported cases, where there was a relatively short history of renal failure, is it known whether the presence of breast calcification preceded the diagnosis of renal disease. With the large increase in mammographic examinations following the institution of the National Breast Screening Programme, it is possible that further cases of breast calcification may be observed in cases of covert renal failure. The finding of bilateral and extensive calcification should provoke further investigation of the patient for possible renal disease. The possibility of a carcinoma should be considered in cases where the calcification is localized or asymmetric.

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The development of an infected false aneurysm following iliac angioplasty

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Keywords: Aneurysm, Angioplasty

Percutaneous transluminal angioplasty is now an established effective treatment for some patients with peripheral vascular disease. The effect of angioplasty is to stretch all layers of the vessel wall which results in splitting of the atheromatous plaque and intima and to some extent the media (Sandborn et al, 1983). Surprisingly, acute arterial rupture and false aneurysm formation at the site of angioplasty are rare complications and few cases have previously been reported (Simmonetti et al, 1983; Samson et al, 1984; Creasy & McMillan, 1987; Moran & Ruttley, 1987). We describe the development of an infected false aneurysm in a patient following iliac angioplasty. As far as we are aware this complication has not previously been recorded.

Case report

A 39-year-old man presented with a 4 year history of claudication affecting both legs, left worse than right. His general health was otherwise good and he was on no medication.

A right transfemoral arteriogram revealed two localized stenoses of the right external iliac artery (Fig. 1), and a 6 cm occlusion of the left superficial femoral artery. Immediately after arteriography the patient underwent angioplasty to both iliac stenoses using a 4 cm long 6 mm inflated diameter polyethylene balloon, and inflation pressures of between 5 and 8 atmospheres. Three thousand units of heparin were given intra-arterially prior to dilatation. A 40 mmHg systolic pressure gradient across the lesions was successfully abolished by angioplasty. The patient was commenced on 75 mg daily of Aspirin and discharged home the following day after an uncomplicated recovery with plans to undertake angioplasty of the left leg at a later date.

He was readmitted to hospital 2 weeks later with a 10 day history of general malaise, frequent night sweats, macroscopic

haematuria on two occasions and increasingly severe right iliac fossa pain.

On examination he was unwell with a pyrexia of 39.5°C and marked tenderness and guarding in the right iliac fossa with an overlying bruit. The right femoral pulse was absent and the leg was cool with poor capillary return. His white cell count was $22 \times 10^9 \text{ l}^{-1}$ and urine and blood cultures proved sterile. An emergency intravenous pyelogram was normal, but an ultrasound scan revealed a 3.5 cm mass in the right iliac fossa with

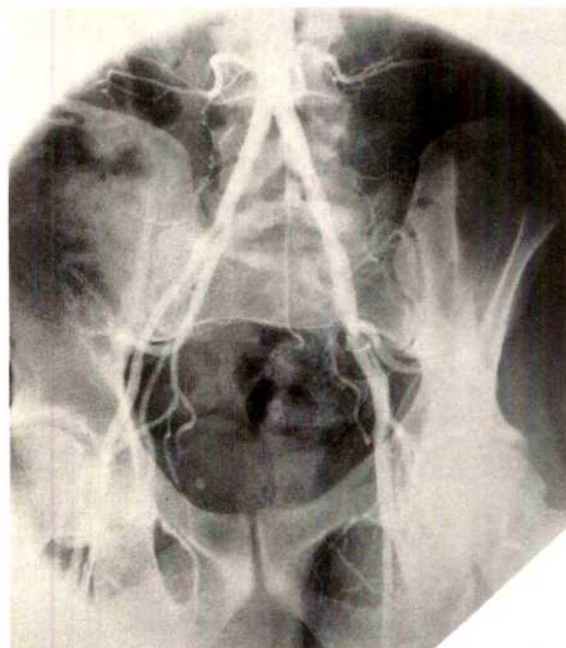


Figure 1. Arteriogram showing two localized stenoses of the (right) external iliac artery.

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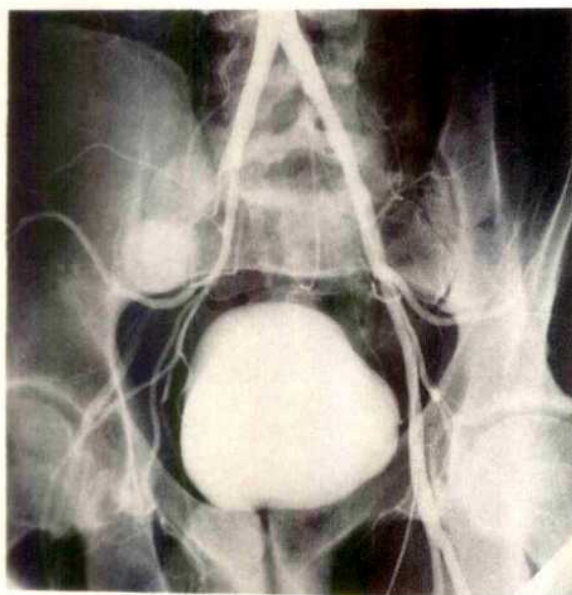


Figure 2. Arteriogram showing a false aneurysm of the (right) external iliac artery.

an arterial signal and visual expansion suggestive of an iliac artery aneurysm. An arteriogram confirmed an aneurysm of the right external iliac artery at the site of previous angioplasty (Fig. 2). At laparotomy a 2 cm longitudinal split in the external iliac artery was found with an associated infected false aneurysm. Thrombus from the aneurysm and part of the disrupted arterial wall were sent for bacteriology. The disrupted segment of the arterial wall was repaired and the external iliac artery tied off proximally and distally. The abdomen was then closed and a left to right femoro-femoral cross-over graft was carried out using an 8 mm externally supported polytetrafluoroethylene (PTFE) (Impra Inc., USA). The patient was placed on intravenous antibiotics for 7 days post-operatively and made an uncomplicated recovery, being discharged from hospital after 10 days, with oral antibiotics for a further 2 weeks. Culture of both the thrombus and the arterial wall revealed a significant growth of *Staphylococcus pyogenes*.

Discussion

Our own experience (Belli et al, 1990) would support the generally held view that percutaneous transluminal angioplasty is a relatively safe treatment for peripheral vascular disease. Nevertheless, this should not allow the clinician to develop a false sense of security, and he should be aware of the possible complications that may arise, however rare. We are not aware of any previous reports of an infected false aneurysm developing at the

site of angioplasty. Only four instances of a non-infected false aneurysm have previously been reported (Samson et al, 1984; Creasy & McMillan, 1987; Moran & Ruttle, 1987), although its true incidence may be higher as follow-up angiography following angioplasty is not routine (Creasy & McMillan, 1987; Moran & Ruttle, 1987).

It is unclear exactly why false aneurysms form following angioplasty but factors such as previous endarterectomy, anti-coagulation, or incorrect balloon size or inflation pressure have been suggested (Creasy & McMillan, 1987; Moran & Ruttle, 1987). None of these factors could be implicated in our case, however, where there was no departure from our usual technique (Belli et al, 1990). One explanation could be that a bacteraemia occurred at the time of the procedure or some days after it, allowing an infection to settle at the site of intimal disruption and thus weakening the vessel wall further and leading to false aneurysm formation.

Our case illustrates the importance of recognizing the infective nature of the false aneurysm. We believe that surgeons should be aware of the possibility when treating this condition, so that ligation of the aneurysm and extra-anatomical by-pass grafting is carried out rather than simple repair of the artery, which we feel would be inappropriate treatment.

Acknowledgments

We thank Mr C. L. Welsh for allowing us to report this case, and Mrs O. M. Woods for typing the manuscript.

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Case reports

Primary lymphoma of the urinary bladder

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(Received September 1990)

Keywords: Primary lymphoma, Urinary bladder

Primary lymphoma of the urinary bladder is rare, occurring most commonly in elderly women. This case report documents the clinical and radiological features of such a tumour presenting in a 22-year-old female patient. To our knowledge, this is the youngest reported case.

Case report

A 22-year-old woman presented with a 16-month history of episodic pain in the left loin and suprapubic region and a 6-week history of haematuria, dysuria and urinary frequency. She had lost 2 stones in weight in the preceding year. On physical examination the only finding of note was a palpable mobile mass anterior to and to the right of the cervix uteri.

Intravenous urography revealed a smooth soft-tissue mass occupying the right side of the bladder (Fig. 1); the upper

urinary tract was normal. Ultrasonography (Fig. 2) demonstrated a homogeneous soft-tissue mass arising from, and apparently confined to, the bladder wall. Examination under anaesthetic confirmed the presence of a 6 cm diameter freely mobile mass arising from the bladder, which on cystoscopy was seen to be covered by normal mucosa. The lesion was biopsied endoscopically and histological examination revealed evidence of a centrocytic (B-cell) malignant lymphoma with a diffuse growth pattern, covered by normal transitional epithelium.

Radiographs of the chest and post-nasal space and a computed tomographic (CT) scan of the abdomen and pelvis showed no evidence of extra-vesical disease. Bone marrow examination was also normal. The disease was therefore staged as I_B.

The patient was treated using the VAPEC-B chemotherapeutic regime (Blackledge et al, 1980). This is an intensive weekly treatment using vincristine, adriamycin, etoposide, cyclophosphamide, bleomycin and prednisolone, with myelotoxic drugs alternating with non-myelotoxic ones over an 11-week period. This was followed by a course of telecobalt radiotherapy to the pelvis with a tumour dose of 3000 cGy. Subsequent CT scans have confirmed complete regression and the patient remains well 14 months after her initial presentation.

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Figure 1. Intravenous urogram of the bladder showing a soft-tissue mass arising from the right side of the bladder.

Discussion

Primary lymphoma of the urinary bladder is a very rare condition, representing between 0.15 and 0.2% of



Figure 2. Longitudinal ultrasound scan through the bladder showing a lobulated homogeneous soft-tissue mass arising from, and apparently confined to, the bladder wall.

all lymphomas (Rosenberg et al, 1961; Freeman et al, 1972), and fewer than 50 cases have been reported to date (Aigen & Phillips, 1986). This contrasts with secondary lymphoma of the bladder, which is present in up to 13% of lymphoma patients at post-mortem examination (Gilver, 1971). Primary lymphoma is more common in males than females (Bhansali & Cameron, 1960; Haeney et al, 1985) and it usually presents in the elderly with haematuria, dysuria and urinary frequency (Bhansali & Cameron, 1960; Wang et al, 1969). It has not, to our knowledge, been previously reported in a patient so young.

The tumour arises within the wall of the bladder and often takes a nodular form, usually being covered by normal transitional epithelium. Ulceration into the bladder lumen may occur, but is not a prominent feature.

The radiological features are non-specific, the commonest being the presence of a mass arising from the bladder base on urography. Ureteric obstruction may occur, but is not common (Binkovitz et al, 1988). To our knowledge the sonographic features have not been described previously; the presence of a solid homogeneous mass within the wall of the bladder, as was found in this case, is probably typical.

Various therapeutic techniques have been used to treat this condition; they include radical cystectomy (Wang et al, 1969), radiotherapy (Bhansali & Cameron, 1960) and chemotherapy (Haeney et al, 1985). In current practice the latter two used alone or in combination are the treatments of choice. The prognosis is relatively good and aggressive local therapy is associated with prolonged survival (Haeney et al, 1985),

although the outlook for a case presenting at this age is unknown.

Acknowledgment

We thank Mr J. Garland for permission to report this case.

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Case of the month

A soldier with recurrent back pain

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A 39-year-old man presented with acute lower back pain referred down the back of the right leg to the knee.

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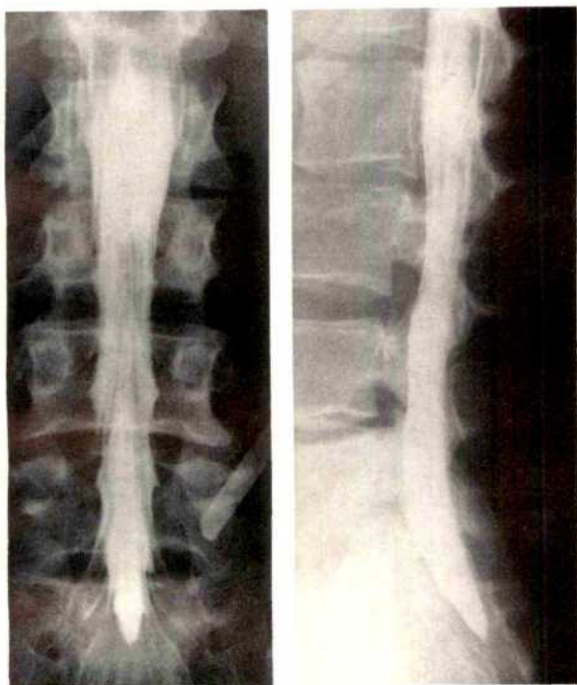


Figure 1. Lumbar radiculogram. Antero-posterior and lateral views.

There were no abnormal neurological findings and clinical examination was unremarkable. He had a long-standing history of recurrent back pain, which had required hospitalization in the past. Lumbar spine radiographs 3 months previously appeared normal. In view of these symptoms and past history, a radiculogram (Fig. 1) and subsequently a computed tomographic (CT) myelogram of the lumbar spine were performed (Fig. 2).

What are the abnormal findings and what is the most likely diagnosis?

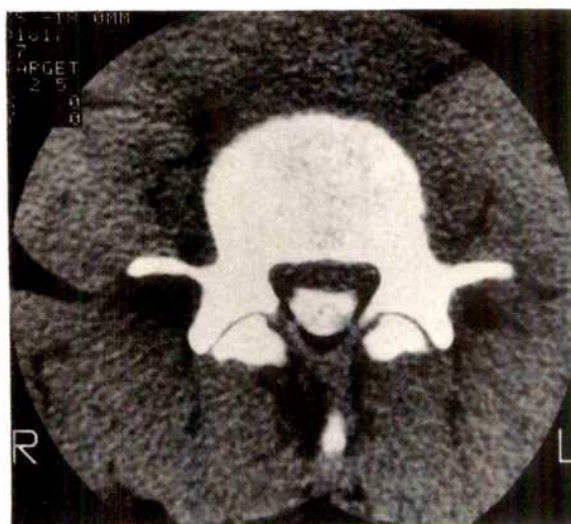


Figure 2. Computed tomographic myelogram of the lumbar spine (L4 level).

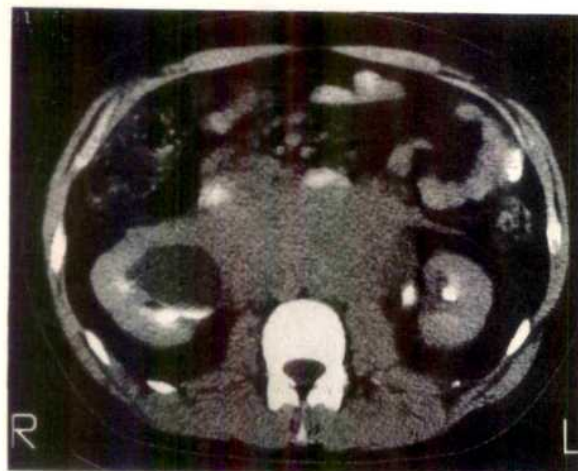


Figure 3. Computed tomographic scan of the upper abdomen showing a large retroperitoneal soft-tissue mass with associated hydronephrosis.

The radiculogram shows the theca being compressed anteriorly by a large soft-tissue mass within the spinal canal extending from L2 to L5. There has also been partial destruction of the vertebral body of L3.

The CT myelogram confirms the radiculogram findings but also shows obliteration of the normal retroperitoneal structures anterior to the vertebral body. In particular, the aorta and inferior vena cava cannot be identified. Abdominal CT (Fig. 3) reveals a large retroperitoneal soft-tissue mass with associated hydronephrosis. Chest CT showed retrosternal lymphadenopathy. Blood samples taken on admission showed abnormal liver function with a Gamma Glutamyl transferase of 176 i.u./l and alkaline phosphatase of 214 i.u./l. His erythrocyte sedimentation rate was raised at 56 mm/h.

These findings are most likely to be due to a non-Hodgkin's lymphoma and subsequent lymph node biopsy confirmed the diagnosis.

Discussion

Spinal epidural involvement is an uncommon initial presentation of non-Hodgkin's lymphoma occurring in only 2.2–3.4% of cases (Levitt et al, 1980; Epelbaum et al, 1986). Although primary spinal epidural

lymphoma has been reported, the majority have disseminated disease (Green et al, 1987). Local back pain, often appearing months before cord compression, occurs as a prodromal symptom in 80% of cases (Epelbaum et al, 1986). Spinal epidural lymphoma has been described in children but 80% occur in adults aged above 40 years of age (Epelbaum et al, 1986).

The commonest site for initial presentation as spinal epidural lymphoma is the thoracic spine. Cord compression at the cervical level has not been reported as an initial presentation probably because cervical lymphadenopathy is noted prior to the spinal canal becoming involved.

Plain radiography shows associated vertebral involvement in between 40 and 60% of cases (Verda, 1944; Bucy & Jerva, 1962; Haddad et al, 1976; Rao et al, 1982). The features are either of pedicle erosion or vertebral destruction with associated compression fracture and paravertebral soft-tissue mass.

Myelography in spinal epidural lymphoma usually shows complete obstruction to the flow of intrathecal contrast medium at the level of the tumour. This case is unusual in this respect, the tumour causing no such obstruction and only anterior thecal displacement.

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Keywords: Spinal, Epidural, Extradural, Lymphoma

Short communications

Body composition by intercomparison of underwater weighing, skinfold measurements and dual-photon absorptiometry

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(Received July 1990 and in revised form October 1990)

Keywords: Lean body mass, Body composition, Absorptiometry, Body density

Since Stern (1901) and Behnke (1961) introduced their techniques for densitometry by submersion, many other methods have been described to estimate body composition in men, ranging from simple to very complex (Siri, 1956, 1961; Garrow, 1982). None of them meets all the desirable criteria: cost, ease of operation and accuracy.

Dual-photon absorptiometry (DPA) is based on measurements of radiation transmission of two separate photon energies through a medium consisting of two different materials, bone and soft tissue. The dichromatic beam from a gadolinium-153 source, with photon energy peaks at 44 and 100 keV, can be used for this purpose. Dual-photon absorptiometry allows measurements on hitherto inaccessible body areas (Peppler & Mazess, 1981).

The present study was designed to validate DPA as an alternative technique for the assessment of the lean body mass and the percentage fat.

Subjects and methods

The subjects were 10 healthy volunteers, six males and four females, aged 22–27 years. Height and weight of the participants were determined. Body density measurements were performed by the underwater weighing technique, based on the law of Archimedes. This method has been described in detail elsewhere (Siri, 1956; Behnke & Wilmore, 1974; Katch & McArdle, 1980). The residual lung volume was simultaneously measured, using the closed-system helium dilution method with a Meinhardt volutest (Siri, 1956; Behnke & Wilmore, 1974). To approximate the air volume of the gastrointestinal tract, a constant correction of 150 ml was accepted (Leusink, 1972; Biersteker et al, 1983).

The second standard type of body density assessment consisted of the determination of the skinfold thickness at four different sites: biceps, triceps, subscapula and supra-iliaca (Durnin & Womersley, 1974; Lohman, 1981). The instrument used for this purpose was the HERO (Harpenden electronic read-out) skinfold caliper (Jones & Marshall, 1979). Body density of each individual was calculated using the regression formula of Durnin and Womersley (1974)

men: $D = 1.1631 - 0.0632 \times \log \sum 4Sf$

women: $D = 1.1599 - 0.0717 \times \log \sum 4Sf$

After submersion densitometry and estimation of body density by anthropometry (skinfold determinations), body fat was

calculated using the equation of Siri (1956):

$$\text{Percentage fat} = \frac{4.95}{D} - 4.5$$

Fat-free mass was obtained as the difference between body weight and body fat (Katch & McArdle, 1980).

$$\text{Fat (kg)} = \frac{\% \text{ fat} \times \text{total body weight (kg)}}{100}$$

Fat-free mass (kg) = Total body weight (kg) – fat (kg)

Finally, total body mineral (TBBM) was measured by DPA using the Lunar DP4-A software version 1.2. The principle and method have been described earlier (Peppler & Mazess, 1981). Lean body mass and percentage fat were deduced using the following formulae:

$$\text{TMst (DPA)} = \text{Weight (DPA)} - \text{TBBM (DPA)}$$

(TMst = total mass of soft tissue)

$$\text{LBM (DPA)} = \text{LBMst} + \text{TBBM}$$

(LBMst = lean body mass of soft tissue)

$$\text{Fat (DPA)} = \text{Weight (DPA)} - \text{LBM (DPA)}$$

$$\% \text{ Fat (DPA)} = \text{Fat (DPA)} / \text{Weight (DPA)} \times 100$$

Results

Calculations of correlation coefficients between the three kinds of measurements and linear regression analysis were performed for mean percentage fat and fat-free mass. The significance of correlation coefficients was tested by variance analysis.

Individual data are given in Table I. The percentage fat had a mean value of 22.8% by submersion, 22.0% by skinfold measurements and 17.8% by DPA. The fat-free body or lean body mass had a mean value of 54 kg by the submersion and skinfold estimation and 61 kg by the DPA.

The correlation between the three methods of determining fat and fat-free mass are summarized in Table II. There is a highly significant correlation of 0.99 between the measurements for fat-free mass. The correlation between submersion and skinfold for percentage fat is higher than between DPA and submersion or skinfold thickness.

Because there is a close correlation between the three measurements of percentage fat, the 5% difference between

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Table I. Values in 10 normal subjects

Subject	Sex	Age (years)	Height (cm)	Weight (kg)	Submersion		Skinfold		DPA			
					% Fat	FFM (kg)	% Fat	FFM	TBBM (kg)	% Fat	LBM	TBBM/% LBM (kg)
1	M	27	200	88.0	14.1	75.6	13.6	76.1	3.811	6.9	86.4	4.4
2	M	25	177	69.0	20.4	54.9	19.0	55.9	2.747	13.3	65.1	4.2
3	M	24	170	69.5	17.8	57.1	17.7	57.2	3.104	12.5	64.6	4.8
4	M	26	183	73.6	14.7	62.8	13.8	63.8	3.160	12.2	70.2	4.5
5	M	24	172	75.5	21.6	59.2	20.9	59.7	3.212	19.1	66.0	4.9
6	M	24	171	67.1	25.6	49.9	23.6	51.3	2.341	21.9	56.0	4.2
7	F	22	174	63.8	23.5	48.8	25.8	47.4	3.085	16.4	57.4	5.4
8	F	25	167	68.0	30.1	47.5	29.1	48.2	2.883	23.7	55.5	5.2
9	F	26	169	60.3	28.3	43.3	26.5	44.3	2.468	24.7	49.4	5.0
10	F	25	167	54.1	31.6	37.0	30.4	37.6	2.201	27.2	42.2	5.2

FFM = fat free mass; TBBM = total body bone mineral; LBM = lean body mass.

percentage fat measured by DPA compared with the two other methods must be due to systematic error in accuracy. The deviation can be expressed as a function with the following formula: $\Delta x = 7.85 - 0.16y$ ($x = \% \text{ fat with skinfold and DPA}$, and $y = \% \text{ fat with submersion}$). The measured value of percentage fat with DPA augmented with Δx values gives the actual real value of percentage fat. As shown in Fig. 1, a decrease in deviation was noticed with increasing percentage body fat.

Discussion

The present study showed a very high correlation between the results for fat and fat-free mass obtained by the standard methods: submersion and skinfold thickness, and DPA. The DPA method, however, underestimates the actual fat by 5%.

According to the manufacturer of the DPA system used, Lunar DP4-A, the difference is a direct consequence of calibration. To date there have been three reports on the same topic (Mazess & Peppler, 1984; Hassager et al, 1989; Wang et al, 1989). The authors recognized that their DPA-measured fat percentage is significantly lower than that estimated by underwater weighing, and by the anthropometric method of Durnin and Womersley (1974), a finding that differs from the results in the literature.

The advantage of DPA to study body composition is that a direct determination of skeletal mass, as well as the lean and fat contents of the entire body, can be made (Mazess & Peppler, 1984). Most methods for non-invasive measurement of body composition are highly indirect in that they measure particularly elemental or chemical compartments which are assumed to be in relatively invariant relationship to compositional

compartments (e.g. calcium as a fraction of skeletal mass, potassium, water or creatinine as indicators of lean body mass) (Mazess & Peppler, 1984). Even newer composition approaches, including those using activation analysis, are highly dependent on such assumptions. One of the basic tenets of compositional analysis from body density is that the composition and densities of major components (skeleton, muscle, adipose) are constant and that skeletal and muscle mass are in a constant ratio (Siri, 1956). In our study of young adults there

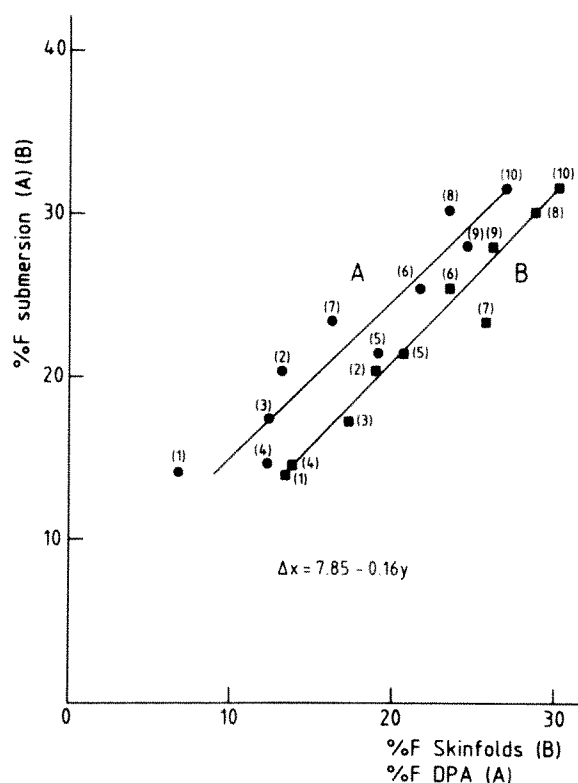


Figure 1. Percentage fat with submersion versus percentage fat with skinfold measurements and DPA.

Table II. Correlation coefficients (R) — standard errors of estimate (SEE)

	% Fat		FFM	
	R	SEE	R	SEE
Submersion and skinfold measurements	0.9808	1.61	0.9975	0.74
Submersion and DPA	0.9578	1.68	0.9935	1.18
Skinfold measurements and DPA	0.9162	2.28	0.9891	1.53

was no constancy in the TBBM as a percentage of LBM; the mean value for TBBM as a percentage of LBM was 4.8%, but it varied from 4.2 to 5.4%.

The assumption of compositional constancy, while reasonable on the average, does not hold in the individual case. The potassium and water content of muscular tissue changes with aging and with disease (Behnke, 1961) and skeletal mass decreases with aging (and with osteoporosis) to a greater extent than muscle catabolism (Allen & Krzywicki, 1961). In particular, variations in skeletal mass must necessarily obfuscate the interpretation of body determination (Allen & Krzywicki, 1961; Baker, 1961), thereby invalidating all those more indirect approaches that had been based on a relationship to body density (Mazess & Pepler, 1984). Total body water (TBW), total potassium (TBK), under water weighting (UWW) and skinfold thickness, the traditional measurements used for estimating fat and LBM, each assumes a constant value in the LBM. Dual-photon absorptiometry provides assumption-free measurements of fat and LBM (with *in vitro* precision of $\pm 1\%$) and thereby established a new framework for studies of body composition (Wang et al, 1987).

Conclusion

Dual-photon absorptiometry provides a measure of body bone mineral, fat and lean body mass that is accurate, relative to other established methods. Accordingly, DPA offers a new opportunity to study the human skeleton *in vivo* and to establish body fat by a method independent from the classical assumption that bone represents a fixed fraction of lean body mass.

Note

The term "lean body mass" was used as a synonym of fat-free mass. However, Behnke's lean body mass differs from the FFM, because the former also includes the non-essential lipids. Behnke defined the lean body mass as the whole body minus non-essential lipids (Siri, 1956, 1961).

Acknowledgments

The authors are grateful to Mrs J. Cartois for secretarial assistance.

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Effect of radiological iodinated contrast media on acetylcholinesterase activity

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Keywords: Contrast media, Acetylcholinesterase, Enzyme inhibition, Ioxaglate

The inhibitory effects of several contrast media on acetylcholinesterase (AChE) activity were studied *in vitro*. Their inhibiting power was in the order: iohalamate > ioxaglate > iopamidol > iohexol. Because both the K_m and maximal velocity (V_{max}) values of the enzyme were altered on adding ioxaglate, the inhibition mode seemed to be of a mixed type. Complete recovery from such inhibition was observed by removing the contrast media from the enzyme. Adding albumin (1%) to the reaction mixture led to a decrease in the inhibitory effect of ioxaglate. These results suggest that the contrast media, which have an inhibitory effect on AChE activity *in vitro*, may have no influence on its activity in blood which contains 4-5% of albumin under physiological conditions.

Radiological iodinated contrast media are relatively non-toxic, but they are employed in such large doses that mild toxic effects are common in clinical practice, and severe reactions sometimes occur (Labbe & Peyroux, 1984; Dawson, 1983, 1985). Since some symptoms of their toxicity such as peripheral vasodilation, bronchospasm and disturbances of cardiac rhythm are similar to those produced by acetylcholine, their inhibitory effects on AChE (acetylcholine acetylhydrolase, EC 3.1.1.7) have been studied (Lasser & Lang, 1966; Dawson & Edgerton, 1983; Howell & Dawson, 1985; Guidollet et al., 1988). The published studies, however, have yielded conflicting results. In this short communication, we report more precisely the nature of the inhibition of AChE by some representative ionic and non-ionic contrast media.

Materials and methods

Contrast agents

The contrast media studied were iohexol (Nycomed Ltd) and iopamidol (Schering Health Care Ltd) as the non-ionic agents and sodium iohalamate (Dai-ichi Seiyaku Co.) and sodium meglumine ioxaglate (Guerbet Co.), a new low-osmolality ionic medium, as the ionic agents.

Reagents

AChE (partially purified from bovine erythrocytes) was obtained from Wako Pure Chemicals Co. (Japan). Intact human erythrocytes from healthy volunteers were also used as a source of the enzyme (Herz & Kaplan, 1973). Human serum albumin (fraction V, 96-99%) was obtained from Sigma Chemical Co. (USA). Acetylthiocholine as a substrate, dithio-bis-2-nitrobenzoic acid (DTNB) as a chromogen and other reagents were of a pure grade.

Method

Erythrocytes were washed with phosphate buffered saline (PBS) (140.5 mM NaCl, 10 mM phosphate buffer, pH 7.4) and resuspended in the PBS. AChE activity was measured by a

colourimetric method (Ellman et al., 1961). Enzyme solution containing DTNB and 0-1% albumin was incubated with varying concentrations of contrast medium (20-160 mg iodine/ml) or with phosphate buffer (0.1M phosphate buffer, pH 8.0, as a control) at 25°C for 10-30 min. After the absorbance at 412 nm had reached a steady state, the substrate was added to the mixture and the absorbance increase for 10 min at 25°C was measured. The procedure in which the intact erythrocytes were used as an enzyme source was as follows: a washed cell suspension (haematocrit value of 0.04%) was mixed with ioxaglate (80 mg iodine/ml) and incubated at 25°C for 10 min. After incubation, an aliquot of the mixture was centrifuged at 1000 g for 5 min, the supernatant was discarded, and then the precipitated cells were washed twice with PBS. The AChE activities in the erythrocytes both before (in the presence of contrast medium) and after washing out the contrast medium were measured.

Results and discussion

The inhibitory effects of the contrast media on AChE activity are shown in Fig. 1. The enzyme activity is plotted against iodine concentration of the reaction mixture as a concentration

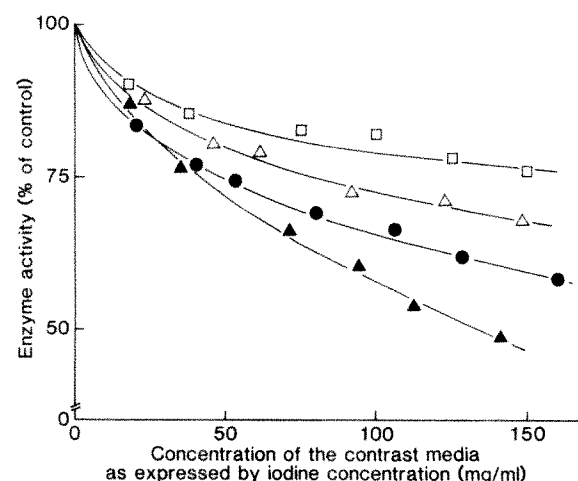


Figure 1. Inhibitory effects of contrast media on AChE activity. AChE (partially purified from bovine erythrocyte) activity determined in the presence of iodinated contrast media (Iohexol, □; iopamidol, △; sodium meglumine ioxaglate, ●; sodium iohalamate, ▲).

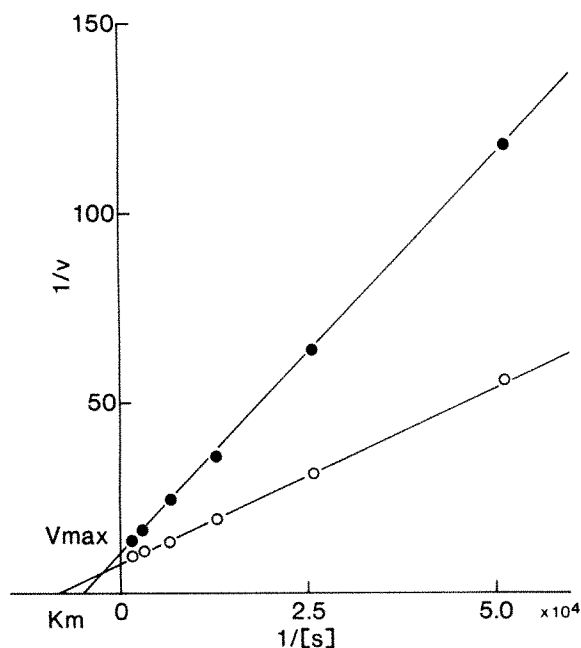


Figure 2. Lineweaver-Burk plot of AchE activity as a function of acetylthiocholine concentration with a constant concentration of sodium meglumine ioxaglate (80 mg iodine/ml, ●) or with phosphate buffer (○).

of the contrast medium (mg iodine/ml). Their inhibiting power was in the order: iothalamate > ioxaglate > iopamidol > iohexol. The results obtained here are in good agreement with those reported previously by Dawson & Edgerton (1983).

Figure 2 shows the Lineweaver-Burk plot of the data from the inhibition studies with ioxaglate. It can be seen that the mode of inhibition was of a mixed type, because both the apparent K_m and V_{max} values were affected on adding ioxaglate. Since ioxaglate and the other contrast media tested are structurally unrelated to the substrates of AchE they probably act by producing a sufficient conformational change of the enzyme protein to reduce, or eliminate, its activity rather than by directly binding to the active site. The inhibitory effects brought about by non-specific binding of contrast media to enzyme molecules have already been reported with several enzymes (Lasser & Lang, 1970a, b, 1971; Canillot et al, 1983; Guidollet et al, 1988).

Binding of the contrast media to serum proteins, not only to some enzymes but also to albumin molecules, has been reported (Lasser et al, 1962). If such binding of the contrast media to both albumin and AchE is non-specific, addition of albumin to the reaction mixture containing the contrast media would suppress their inhibitory effect on AchE activity. Figure 3 shows the effect on the inhibition of AchE by ioxaglate when albumin was added. A marked depression in its inhibitory effect was observed in the presence of albumin at a concentration of 1% or less. The reduced inhibition may result from a decrease in the number of molecules of the contrast medium bound to the enzyme protein because of the presence of a large number of albumin molecules. It is possible that such easy binding of these contrast media to macromolecules in the body may cause toxicity. These results, however, also suggest that they may not actually suppress AchE activity in blood

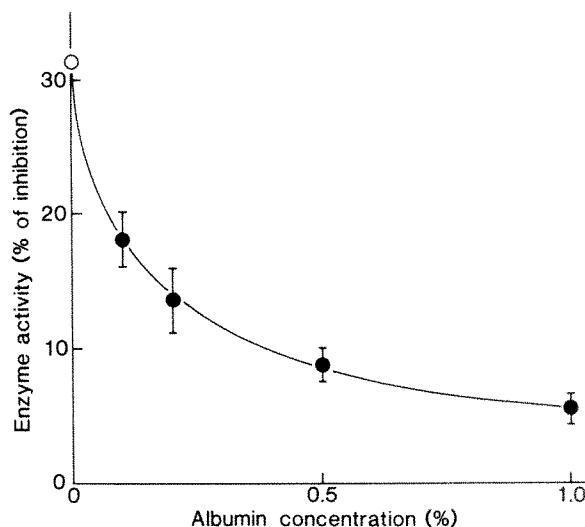


Figure 3. Influence of albumin addition on the inhibitory effect of a contrast medium on AchE activity. AchE activity in a solution containing sodium meglumine ioxaglate (80 mg iodine/ml) was determined in the presence of human serum albumin (0.1–1.0%).

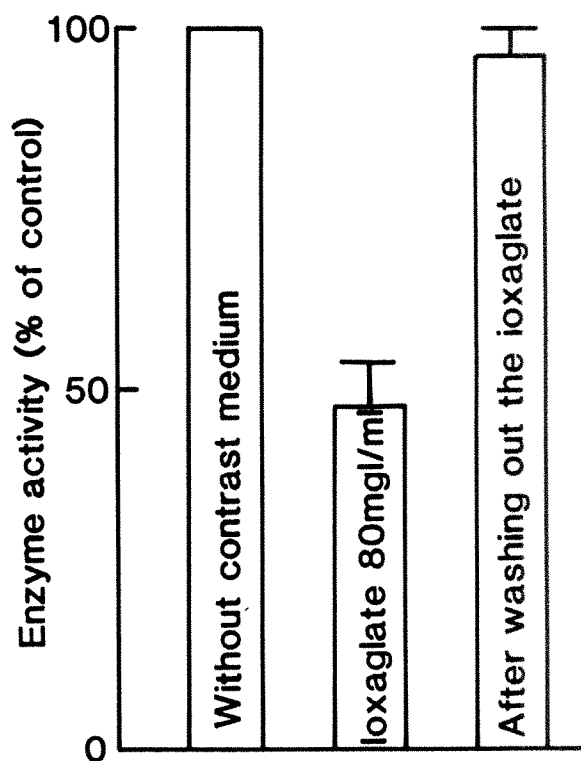


Figure 4. Reversible inhibition of AchE activity by a contrast medium. AchE activity bound to human erythrocyte membrane was determined in the absence (control, left column) or presence of sodium meglumine ioxaglate (80 mg iodine/ml, centre column), and after washing out the contrast agent with isotonic saline solution (right column).

under physiological conditions where albumin molecules are far more abundant than enzyme molecules.

Finally, reversibility of the AchE inhibition by contrast medium was examined. For this human intact erythrocytes were used because the cells have AchE on their surface (Herz & Kaplan, 1973) and can be easily separated from the contrast medium by mild centrifugation. As shown in Fig. 4, about 50% of the AchE activity in erythrocytes was inhibited on adding ioxaglate (80 mg iodine/ml). On removing the agent from the erythrocyte suspension, however, the enzyme activity reverted completely to the original level. This suggests that, even if a decrease in AchE activity occurs *in vivo* following an injection of contrast medium, reversal must readily take place with a decrease in the body fluid's concentration of contrast medium.

Conclusion

Contrast media, especially ionic contrast media, brought about a reversible decrease in AchE activity with a mixed mode of inhibition. However, addition of 1% albumin prevented the decrease in AchE activity by the contrast media, suggesting that no appreciable inhibition of AchE activity occurs in blood containing injected contrast medium under physiological conditions.

Acknowledgment

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

The significance of patient weight when comparing X-ray room performance against guideline levels of dose

THE EDITOR—SIR,

On the basis of a national survey (Shrimpton et al, 1986) of doses to adult patients from routine X-ray examinations, the National Radiological Protection Board (NRPB) has formulated a set of guideline entrance surface doses for some common radiographic projections. These guideline doses are shown in Table I. They have been recommended by a joint working party of NRPB and the Royal College of Radiologists (RCR) as a useful step in reducing unnecessary medical exposures (RCR & NRPB, 1990). The doses were set at the third quartiles of the exposures found in the national survey, *i.e.* 75% of radiography rooms achieved a mean dose lower than each guideline. It is suggested that radiography departments observing levels of mean dose for an X-ray room that are close to or above the guideline doses should undertake a thorough review of radiographic practice, in order to bring their doses more into line with the majority. Attainment of doses just below the guideline levels, however, should not be construed as achievement of optimum performance, since further dose reductions may still be reasonably practicable.

The performance of an individual X-ray room for an examination may be compared with the guideline dose by measuring, with thermoluminescent dosimeters (TLDs) for example, the mean entrance surface dose for a sample of 10 or more patients of typical physique (with a weight in the vicinity of 70 kg). Despite selecting patients in this way one often finds that the mean weight of the sample differs from the typical patient weight of 70 kg. In the national survey, where no restrictions were imposed upon patient weight, the range of mean weights for rooms with 10 or more patients varied by about ± 10 kg around the figure of 70 kg. A method has therefore been developed to provide an indication of the significance of such variation in weight for X-ray examinations of the trunk.

Table I. Guideline values of entrance surface dose per film (including backscatter) for a standard 70 kg patient

Examination	Projection	Guideline dose (mGy)
Skull	AP/PA	5
	Lat	3
Chest	PA	0.3
	Lat	1.5
Thoracic spine	AP	7
	Lat	20
Lumbar spine	AP	10
	Lat	30
	LSJ	40
Abdomen	AP	10
Pelvis	AP	10

Abbreviations: AP=anteroposterior; PA=posteroanterior; Lat=lateral and LSJ=lumbosacral junction.

The method relies on the fact that many of the variables that affect patient dose remain constant when one considers individual radiography rooms. For instance, the speed of the film-screen combination and other equipment parameters that are not routinely selectable do not generally change from radiograph to radiograph when taken in the same room. Under these circumstances, the selection of exposure factors according to the thickness of the part of the patient that is undergoing X-ray imaging will be a key determinant of the dose. In this analysis the weight of the patient was assumed to be correlated with the thickness of the trunk.

A simple linear relationship between patient weight and entrance surface dose was found to provide the best fit to the data rather than a quadratic or cubic relationship. (There was a mean correlation coefficient for all the rooms of 0.6 between weight and dose). Such a linear relationship can be described by the equation

$$\text{Entrance surface dose} = A \cdot \text{weight} + B$$

Values of *A* and *B* relating to individual radiography rooms in the national survey have been calculated for each projection where there were measurements on 10 or more patients. Not surprisingly, the slope *A* and constant *B* were different for different rooms and for different examinations and projections. The values of *A* were always positive, that is, the trend was for dose to increase with an increase in weight.

Firstly, the effect of correcting data from the survey to allow for deviations in mean patient weight was determined. The equation that was established for each room was used to correct the mean dose for that room to that appropriate for a patient weight of 70 kg. It was found that the third quartiles of doses corrected in this manner would have been rounded to exactly the same values as the uncorrected guideline doses. Therefore, adjusting for the influence of patient weight would not have altered the present levels of guideline dose.

Secondly, the mean values of *A* and *B* over all rooms in the survey for each projection were calculated to establish typical correction factors for the entrance surface dose as a function of mean patient weight. The second column of Table II shows the mean trend between dose and weight observed for each projection, expressed as the percentage change in the dose from that for a standard 70 kg patient per unit change in weight. The third and fourth columns show the minimum and maximum values determined for individual rooms. Dose-weight adjustments observed for each X-ray projection range from less than 1% per kg to over 3% per kg between X-ray rooms, with changes in dose of about

Table II. Dose-weight adjustments

Projection	Percentage change in dose per unit weight (% per kg)		
	Mean	Minimum	Maximum
Chest PA	1.7	0.8	3.3
Abdomen AP	2.1	0.8	3.1
Lumbar LSJ	1.6	0.5	2.7
Pelvis AP	2.1	0.7	3.7
Thoracic AP	1.2	0.3	3.3

2% per kg being typical for all examinations considered. For the national survey, 44% of rooms would have required a correction to the mean dose of less than 5%, whereas 29% would have needed 5–10%, and 27% would have required 10–20%. The range of corrections could be expected to be much more restricted than this if individual X-ray departments are more selective in their measurement sample by excluding extremely large or small patients.

In summary, if dose measurements are limited to a sample of typical patients whose mean weight lies within 5 kg of 70 kg, any correction to the mean dose to make it appropriate for a 70 kg patient is unlikely to exceed 15% and on the average will be less than 10%. This level of correction can be regarded as insignificant in the context of checking performance against the guideline doses and can be ignored.

Yours, etc.,

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Occupational exposure and the Central Index of Dose Information

THE EDITOR —SIR,

The paper by Kendall and Hughes (1990) provided interesting background information on the Health and Safety Executive (HSE) Central Index of Dose Information and occupational exposure levels. However, such has been the pace of events in the field of dose reduction in recent years, that dosimetry data rapidly become superseded.

Thus, readers may wish to note the following information which relates to BNFL employees on the Sellafield Site (which includes Calder Hall but which is dominated by fuel reprocessing).

	1986	1987	1988	1989
Total number of workers (1)	6000	6400	6500	6500
Workers exceeding 15 mSv per annum (1)	840	590	400	270
Annual collective dose (man Sv) (2)	38	32	30	23
Average annual dose (mSv) (2)	6.3	5.0	4.6	3.5

Notes: (1) Rounded as per Kendall and Hughes and (2) presented to 2 significant figures.

All data are, of course, the sum of the external dose and the committed effective dose equivalent from intake of radionuclides. As can be clearly seen, significant reductions in average and collective dose have been achieved together with the numbers of employees in the upper dose range.

Yours, etc.,

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Book reviews

MRI Physics for Physicians. By Alfred L. Horowitz, pp. xii + 113, 1989 (Springer-Verlag, New York), DM38. ISBN 0-387-96904 (New York) 3-540-96904-7 (Berlin)

and

A Non-Mathematical Approach to Basic MRI. Ed. by H. J. Smith and F. N. Ranallo, pp. vi + 203, 1989 (Medical Physics Publishing Corp., USA), \$35.00. ISBN 0-944838-02-2

For those, like me, whose numeracy is sub-optimal, the advent of nuclear magnetic resonance imaging and spectroscopy has been disquieting. The concepts, if not the detailed technicalities, of computed tomography and ultrasound were relatively easy to cope with but not so with magnetic resonance. These two paperback volumes are designed for those of us whose mathematics is rudimentary. The task is considerable and even though the mathematical content of these books has been reduced the concepts still remain quite difficult to grasp, certainly at first reading.

The book by Dr Horowitz is essentially confined to physics and, in some ways, is less comprehensive than the book by Smith and Ranallo. Essential concepts are more easily understood in *MRI Physics for Physicians*, but a better overall understanding would be achieved through the other book.

For those of us who find the concepts heavy going and who need many bites of the cherry, a reasonable approach could well be to start with the Horowitz book and then graduate to the other. I suspect a lot of us, honestly, will still have to profess a considerable ignorance. They would, however, at least have tried.

D. G. SHAW

Atlas of Slices of the Temporal Bone and Adjacent Region Anatomy and Computed Tomography. By Henri Sick and Francis Veillon, pp. viii + 161, 1988 (J. F. Bergmann Verlag, Munchen), DM228.

ISBN 3-8070-0370-3 (Bergmann)
0-387-00370-3 (Springer, New York)

Three-dimensional reconstructive imaging may have a place for maxillo-facial and plastic surgery of the face, but it has little relevance for the study of the petrous temporal bone, for which a comprehensive knowledge of sectional imaging is essential. Comparison of sectional imaging, with equivalent post mortem anatomical sections, is such an obvious exercise that it is not surprising that many such works have been produced since tomography was first described more than 50 years ago. However, it is only recently that computed tomography (CT) has achieved a degree of spatial resolution that enables fine detail to be identified, especially of small structures, in the petrous temporal bone.

This latest large atlas by a Professor of anatomy and a radiologist from Strasbourg must have entailed much time and effort and is probably the best and most comprehensive so far. Unlike some previous works, the superb histological sections are in black and white and clearly labelled with the nomenclature on the same page obviating the need to turn to a "key" at the end. This absence of colour in no way detracts from the quality of the pictures and must be a factor in the not unreasonable price of £75. I very much liked the comparable adult CT sections adjacent to those from a neonate labelled CTN. The labyrinth and middle ears are fully developed at

birth, but during childhood there is a slight alteration in orientation and appearance of the petromastoid, with the development of mastoid pneumatization and ossification of the tympanic ring as well as around the internal auditory meatus. This aspect will be particularly useful for those involved with ENT imaging in children and I would consider this an essential reference book for a children's hospital. The display of comparable CT sections (1 mm thick) with equivalent histology sections (a few microns thick) is not easy. Where the CT scan does not show structures visible on the histological slice, the technical limitations of the former must be considered. This is explained in the good introduction.

For all its excellence, the book did not elicit much enthusiasm amongst radiology trainees who considered it too imposing and detailed. Certainly very careful study of the illustrations is necessary, but for surgeons and radiologists with a particular interest in the ear this must be a most worthwhile and essential reference book. However, I cannot recommend it for district general hospitals or for individual purchase when other simpler and more readable works are available.

P. D. PHELPS

Computed Tomography of the Trunk Normal and Pathological Anatomy. By Jacques Hureau and Janine Pradel, pp. 487, 1990 (Piccin Nuova Libreria, Italy).

ISBN 88-299-0731-6

After a brief description of the basic principles of computed tomography (CT), the first half of this book by a surgeon and a radiologist from Paris is primarily an atlas of cross-sectional anatomy, from the level of the thoracic inlet to the perineum. Carefully prepared and meticulously labelled anatomical sections from four different subjects are presented together with a CT scout view demonstrating the level of the section and a number of CT images illustrating abnormalities at the same level. Some normal CT images have also been included but these are presented as "cases" and can only be identified by reference to the index. The quality of the CT images is variable and does not always reach the same high standard of reproduction as the anatomical sections. The authors have perhaps taken on a little too much by endeavouring to include so many (over 300) interesting cases in this part of the book as well as illustrating the normal anatomy. There is scarcely any room for discussion of the clinical setting or CT findings in many of the cases beyond a bare statement of the diagnosis.

The remainder of the book consists of 10 chapters on selected aspects of CT anatomy including the diaphragm, the peritoneal cavity, the retroperitoneal spaces and the thoracic and abdominal walls. There are detailed discussions of pulmonary and particularly hepatic segmental anatomy reflecting the authors' special interest in this field. These chapters are well illustrated but are generally written from the perspective of the anatomist rather than the clinical radiologist. The chapter on the mediastinum, for example, contains no description or classification of lymph node groups. The chapters on the aorta and on post-operative appearances are more clinically orientated and include helpful discussions of representative cases and potential pitfalls. One problem is that the book has been some time in preparation and most of the text was written in 1984; in such a rapidly advancing area of medical imaging this inevitably results in a few statements, particularly about the limitations of CT, which would no longer be considered valid.

Finally, and most unfortunately for the authors, they have been badly let down by the translation from the original French which impairs understanding of the text and renders

much of it quite difficult to read. As an atlas of cross-sectional anatomy this book will bear comparison with the best of other such works, but as a manual of body CT it is unlikely to be widely used in this country.

G. F. Maskell

Essentials of Body Computed Tomography. Ed. by K. Gedgaudas-McClees and W. E. Torres, pp. x+291, 1990 (W. B. Saunders Company, Eastbourne), £39.50. ISBN 0-7216-8890-X

This is a relatively short text book (290 pages) the purpose of which is to provide "a 'bridge' . . . to help cover the ground between the very basic material presented in student text books and the lengthy material currently available in books on computed tomography". It has to be asked whether the author's perception of a need for such a "bridge" is correct. This book is certainly too detailed for medical students. A radiologist in training preparing for Part I FRCR or similar examinations can obtain the information on anatomy and techniques contained in this book by reading the introductory sections on each part of the body in larger books on computed tomography (CT) scanning. Radiologists preparing for Part II FRCR need something more detailed. Practising radiologists and clinicians are unlikely to read a whole text book on CT and are better served by a reference book, which again needs to contain more information than this relatively small volume.

If we assume that there is a readership for this type of book, the next question to be asked is whether the authors have accomplished the task they have set themselves. The book has 13 chapters. The first chapter covers the basic principles of CT scanning and the second one the normal anatomy of the chest and abdomen. The next ten chapters are concerned with individual organs and parts of the body and describe pathological conditions affecting those areas. The final chapter provides an overview of CT-guided interventional radiology.

The book reads well and despite the fact that there are seven contributors, there is very little repetition which is to the credit of the editors. Inevitably, there is a certain lack of uniformity. For example, in the chapter on "computed tomography of the normal chest and abdomen" the method of examination of abdominal organs is described. However, in the chapter on the spleen the technique of examining that organ is described in more detail, whereas in the chapter on the pancreas there is simply a statement that "the techniques of evaluating the pancreas have been outlined in the chapter on the normal anatomy of the abdomen". A result of this lack of uniformity is that in the book as a whole, insufficient details are given about how to scan the pancreas.

The quality of the illustrations is not particularly good for a text book published in 1990. Nevertheless, the points illustrated are relevant and important and the number of illustrations is appropriate for each chapter. A relatively large number of references is given in each chapter and it can be argued that this is not appropriate for this type of book. A radiologist or clinician who is likely to refer to the articles quoted in the references is also likely to acquire a larger text book. Most of the references are rather old and several chapters do not mention any articles published after 1987.

The book is rather out of date in certain areas and inconsistently so: in the chapter on the spleen, mention is made of EOE-13, an experimental oily contrast agent and yet in the chapter on the mediastinum, pulmonary hila and lungs there is hardly a mention of the enormous advances made, in recent years, on the CT findings of diseases affecting the lung parenchyma, an area in which CT is now an essential part of the investigation of patients.

In summary, this book is pleasant and easy to read but with no easily identifiable readership. The authors have set themselves an impossible task by aiming to cover an enormous subject in such a small book. The result is that the gaps are too great for me to recommend that this text book should be purchased by radiologists. Clinicians who have an interest in CT would benefit from reading it, but they would be better advised to buy a book of similar size devoted to their area of interest rather than a rather superficial general text book.

E. J. ADAM

CT and MRI of the Thorax. Ed. by E. A. Zerhouni, pp. x+222, 1989 (Churchill Livingstone, New York), £47.50. ISBN 0-443-08602-8

This is the second volume in the excellent Churchill Livingstone series *Contemporary Issues in Computed Tomography* and it is edited by an acknowledged leader in the field of lung computed tomography (CT). With certain notable exceptions all contributors, like the editor, are from Johns Hopkins School of Medicine.

The book is compact, running to about 200 pages and 330 references, with good quality illustrations. There are nine chapters in all devoted to either CT or CT and magnetic resonance imaging (MRI) of the chest. Some chapters are disease oriented (*e.g.* lymphoma, immuno-compromised host) and others compartment oriented (*e.g.* airways, diaphragm, etc.). Chapters are basically short "state of the art" reviews, some contrasting and comparing CT and MRI. Some chapters are more up to date than others, with references essentially up to 1986 in some and to 1988 in others. It is not surprising that dealing with the chest the balance of the book is tipped towards CT. There are particularly good chapters on an overview of CT and MRI chest imaging (W. R. Webb), high resolution CT in diffuse disease (E. A. Zerhouni), CT and MRI of the airways (D. P. Naidich) and MRI and lymphoma (Richmond and Zerhouni). The book ends with five rather ordinary studies.

I can enthusiastically recommend this book to radiology departments and particularly those that teach. In the latter I hope it will join the other ten volumes in the series. You must however go out and buy the book now as this is a very rapidly changing field.

A. G. WILSON

Maxillofacial Imaging. By Angelo M. Delbaso, pp. xvi+799, 1990 (Harcourt Brace Jovanovich Ltd, London), £84.00. ISBN 0-7216-2315-8

The maxillofacial region is a radiological no-man's land in which few general radiologists have any special interest or knowledge and even ENT radiologists with considerable expertise in assessing the nose, sinuses and pharynx can have problems with lesions of dental origin. Radiologists with a special interest in malignant disease are often expert in the staging of malignant tumours arising in the maxillofacial region but are less expert in the diagnosis and assessment of non-malignant conditions. Dental radiologists have great experience in plain film radiography and panoramic radiography of the teeth and associated structures but few, even those with the new Diploma of Dental Radiology, have much experience of computed tomography (CT) scanning or malignancy.

Maxillofacial Imaging, edited by a radiologist qualified in medicine and dentistry, aims to cover this difficult region. The maxilla, mandible, temporo-mandibular joint, salivary glands,

nose, paranasal sinuses, pharynx and para-pharyngeal region are comprehensively covered. There are also chapters on cervical spine injuries, the orbit, swallowing and the role of radiotherapy in the treatment of head and neck tumours. This is a multi-author book, with 31 contributors, which suffers from the attendant disadvantage of some overlapping contributions, but there is a substantial advantage in that the text and references are more up to date than could ever be achieved by a single author. The ideas expressed are middle of the road and the index is good, which are important advantages in a text likely to be used for reference.

The book is copiously illustrated and most of the illustrations are of a very high quality. There are magnetic resonance imaging (MRI) images in many chapters, with two chapters devoted entirely to MRI which could not have been written in the UK as the MRI images are simply not available. There are some excellent line diagrams especially those on face fractures and the temporo-mandibular joint. There are CT images in most chapters and there is an excellent account of panoramic zonography which describes the technique and its artefacts.

Some of the CT scans must have been taken some years ago as the resolution is less than would be obtained with modern equipment. The field size of some illustrations is excessively large so that the area of interest becomes quite small. This is particularly noticeable in some MRI images of the temporo-mandibular joint, where the displaced temporo-mandibular disc measures 4×1 mm and can be difficult to find in an image measuring 7×7 cm. The legends are long and sometimes extend to the next page which makes the book difficult to read in some places. It is easy to criticize however and I hope that these minor faults will be corrected in subsequent editions.

Maxillofacial Imaging is likely to become a standard text on modern techniques as they apply to the maxillofacial region and I can recommend it as being better illustrated, more comprehensive and more up to date than other currently available books on the same subject.

JAMES MCIVOR

Imaging of the Liver, Pancreas and Spleen. Ed. by R. A. Wilkins and H. B. Nunnerley, pp. ix + 557, 1990 (Blackwell Scientific Publications, Oxford), £110.00.
ISBN 0-632-02609-X

This book comprehensively covers "state of the art imaging" of the liver, pancreas, biliary tree and spleen. There is a refreshing spectrum of contributors from the length and breadth of the United Kingdom. It is well produced, easy to read and has a modern style. There are occasional algorithms which are especially useful. The illustrations are particularly excellent throughout with relevant labelling although some of the ultrasound images are rather out-dated. The references are numerous and up to date and the book is adequately indexed.

There are 30 chapters in all. These are divided into six parts comprising the normal liver, liver disease, biliary system, pancreas, spleen and abdomen with the liver chapters occupying roughly half the 542 pages. All modern imaging methods are discussed including magnetic resonance imaging (MRI). Paediatric disease is also well represented. The abdominal section comprising of three chapters (MRI of the pancreas and spleen, trauma of the upper abdomen and an approach to abdominal masses) appears rather untidy in format but not content and could perhaps have been better incorporated under the main headings.

Some of the chapters are multi-authored and inevitably there are overlaps in factual information and stark differences in

style but this does not detract from the general quality. Each encompasses a particular area of expertise e.g. "circulatory changes in liver disease" and is a change from the all embracing works of the standard textbooks. A chapter exclusively devoted to portal hypertension exemplifies this trend.

The content is necessarily basic particularly in the initial section on the normal liver. Pathological states are covered in more detail. However, like all texts of this length, there is a tendency to omit some of the finer points of information that rarely find their way into print but frequently and unfortunately for the examinee often appear in multiple choice question examinations! A lot of effort has obviously gone into this book not only by all the authors but also by the editors and publishers. Both the radiological trainee and more senior radiological staff will benefit from reading it. The price of £110 is competitive.

SIMON N. JONES.

Aids to Radiological Differential Diagnosis. By Stephen Chapman and Richard Nakielny, pp. xviii + 541, 1990 (Harcourt Brace Jovanovich Ltd, London), £12.95.
ISBN 0-7020-1440-0

This useful pocket guide is aimed mainly at trainee radiologists. Part 1 provides lists of differential diagnoses of radiological signs while Part 2 summarizes the radiological findings in some important conditions. Compared with the first edition, there are new sections on obstetrics and gynaecology, mammography, computed tomography (CT) and nuclear medicine, all of which feature increasingly in the final FRCR. Blank pages at the end of chapters are an additional useful feature.

In Part 1 the lists aim to follow a surgical sieve classification with idiopathic last, even though this may be the commonest cause of the sign in question e.g. cryptogenic fibrosing alveolitis after tuberosc sclerosis in the differential diagnosis of honeycomb lung. The three commonest causes in bold type at the top of the list would be more helpful. The few illustrations are appropriate and instructive. The references have been updated up to 1988 from the previous edition. Although it is a multi-author production, it is cohesive and there is no overlap.

Overall, this book has no competitor in the market. A straw poll of 20 colleagues, all of whom had purchased it, recommended it highly. Used in conjunction with specialized textbooks it is essential reading for postgraduate examinations. Its compact size and economical price make it a valuable white-coat pocket book, not only for the pre-fellowship candidate but also as a handy little reference for the qualified radiologist.

N. DE SOUSA

The Causation and Clinical Management of Pelvic Radiation Disease. Ed. by P. F. Schofield and E. W. Lupton, pp. xviii + 153, 1989 (Springer-Verlag, Berlin), £49.50.
ISBN 0-387-19561-0

This book concerns itself with damage to the gastro-intestinal tract and urinary tract from radiotherapy. There is an introductory part on general principles covering radiotherapy techniques, pathology of radiation injury and the radiological appearances of damaged bowel and urinary tract. There follow chapters on the clinical features, experimental findings and treatment of radiation bowel disease and similarly for urinary tract damage. The authors are all from the Manchester area and are very much calling upon their experience in that geographical area. However, all chapters are well referenced

and the techniques described in radiotherapy, radiology and surgery are in general use.

Each of the chapters is, in general, well written and the interest of the contributing authors shows through in what could otherwise be a rather dull topic. In particular, the chapter on radiological changes and pathological changes are very enthusiastic. I found the book well worth reading, although the style of the chapters is such that they need to be read as a whole and it is difficult to dip into them as reference works. I felt that the book was worth having in a radiotherapy department and should be read by trainees in oncology for the wealth of clinical experience included. There are numerous illustrations of radiological and pathological specimens and the book is well produced. However, at £50 for 150 pages, the book is expensive.

PETER BLAKE

Procedures in Diagnostic Radiology. By Terence Doyle, William S. C. Hare, Kenneth Thomson and Brian Tress, pp. viii + 235, 1989 (Churchill Livingstone, Edinburgh), £12.95.
ISBN 0-443-02982-2

This book covers all of the radiological procedures likely to be requested in a modern hospital, with an emphasis on the practical aspects. Each procedure is described in terms of indications, contra-indications, patient preparation, technique, practical difficulties and complications. The detail in the description of techniques is adequate and many useful practical tips are included. The text is well referenced to direct further reading. Established interventional procedures including angioplasty, percutaneous insertion of biliary endoprotheses, percutaneous gall stone removal and numerous uro-radiological techniques are described.

The book is aimed both at radiology trainees learning how to perform procedures and at practising radiologists as a reference work for those procedures which they may perform on a less than regular basis. Some of the procedures described include aspects of technique which are not normal radiological practice in this country. These include the use of oily contrast medium in antegrade pyelography and the use of large volumes (150 ml) of diluted ionic contrast medium in lower limb phlebography. Pre-testing with intravenous contrast media for patients with an allergic history is suggested early in the text although, later on we are correctly informed that pre-testing is generally believed to be unhelpful. The use of ionic contrast media in arteriography is described as used in the Royal Melbourne Hospital. This, however, is no longer recommended in British practice. These points are likely to cause confusion to radiology trainees.

The book is described as being divided into key body systems. Chapter five, however, is rather confusingly titled "Cerebral Angiography" and yet includes myelography, discography and computed tomography (CT) air cisternography. It would be more aptly titled "The Central Nervous System". Chapter seven includes an assortment of unrelated procedures in a somewhat random sequence. There are many useful line diagrams to illustrate points of technique but on the whole there is a sparsity of radiographic illustrations.

Despite its being very reasonably priced at £12.95, I would not recommend its purchase by radiology trainees. It does not contain sufficient information for the purposes of preparation for the FRCR examination and it is not of handy pocket size suitable for everyday use in the department.

SIÂN E. EVANS

The British Journal of Radiology

Comparison of colour Doppler ultrasound with venography in the diagnosis of axillary and subclavian vein thrombosis

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Abstract. The primary imaging technique in suspected venous occlusive disease has for many years been contrast venography. Recent studies have shown ultrasound with the addition of colour Doppler imaging to be a suitable alternative method in the diagnosis of lower limb venous thrombosis. We have applied these techniques to the upper limb venous system, and have performed a prospective study of 19 patients (30 limbs) comparing colour Doppler ultrasound with venography in the diagnosis of axillary and subclavian vein thrombosis, for which colour Doppler ultrasound has a sensitivity and specificity of 100%. If vein stenosis is included, the sensitivity falls to 89%. We propose that colour Doppler ultrasound is a suitable first-line alternative to venography in the diagnosis of axillary and subclavian vein thrombosis. In addition to showing the major venous drainage of the upper limb, ultrasound routinely assesses patency of the internal jugular vein, which is, on occasion, of clinical relevance when determining possible future sites of venous access. If, however, colour Doppler ultrasound is normal then bilateral upper limb venography is indicated to exclude a more central venous problem or localized stenotic lesion.

Central vein occlusion accounts for 1-2% of deep venous thrombosis (Coon & Willis, 1966). The exact reason for this relatively infrequent occurrence is not fully understood; many theories have, however, been suggested (Prescott & Tikoff, 1979).

Central vein thrombosis may be of two types: primary or secondary. The commonest cause by far is secondary to central vein catheterization and the main method of diagnosis to date remains upper limb venography. The potential hazards of venography are well known and when taken in consideration with the radiation dose and cost of investigation is less than ideal as the primary imaging method.

There has been a search for a suitable non-invasive alternative, particularly studying the lower limb. Techniques that include impedance plethysmography, isotope studies and thermography have all been assessed with markedly variable results questioning the reliability of these techniques (Prescott et al, 1978; Pochaczewsky et al, 1982; Ramchandani et al, 1985; Christensen et al, 1987). Similar findings have been shown in upper limb thrombosis (Sotturrai et al, 1982). Results using B-mode ultrasound with Doppler (duplex ultrasound) in the upper limb are very encouraging (Wing & Scheible, 1983; Gooding et al, 1986; Falk & Smith, 1987).

Since colour Doppler ultrasound has been shown to

have specific advantages in the diagnosis of lower limb venous thrombosis (Baxter et al, 1990), we have performed a prospective evaluation of colour Doppler ultrasound with venography in the diagnosis of central vein thrombosis to determine any specific advantages over conventional imaging. In view of the relatively uncommon nature of central vein thrombosis we studied an "at risk" group of renal dialysis patients, all of whom had had multiple recent subclavian venous cannulations.

Method

Nineteen patients (30 limbs) on long-term renal dialysis were prospectively studied. All patients had signs and symptoms referable to the upper limb, including intermittent oedema, pain and venous distension. All but five of the 19 patients had had two or more central venous lines inserted via the subclavian vein. The male:female ratio was 11:8 and the age range 18-77 years (mean 52 years). Colour Doppler ultrasound and venography were performed separately in all cases by radiologists, both examinations being within 2 hours of each other.

Venography was performed in all cases using digital subtraction angiography (DSA) (Philips). Ten millilitres of iopamidol (Niopam)300 were injected by a 21G butterfly needle in the median antecubital vein. Digital subtraction angiography imaging was begun, on average, after a 4 second delay with a sequence of one image per second for up to 16 seconds, and was performed with the arm in the anatomical position.

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Figure 1. Colour Doppler ultrasound scan in the longitudinal axis demonstrating a normal patent axillary vein.

Venograms were reviewed at a later date by the two radiologists separately. Interpretation of venographic results was in concordance in all cases.

Colour Doppler ultrasound was performed using a 7.5 MHz linear array probe (Acuson 128). The examination was performed with the patient supine and the arm in the normal anatomical position. Scanning began in the infraclavicular fossa, and the subclavian and axillary vein were both identified in their longitudinal and transverse axes (Fig. 1). The accompanying artery was also identified in every case by means of Doppler spectral analysis to prevent confusion between the two vessels. Spontaneous flow was present in all patent venous systems. Responses to respiration, sniffing and Valsalva manoeuvres were noted where possible.

The subclavian vein was then scanned in a longitudinal axis from a supraclavicular approach and followed medially. The internal jugular vein was also imaged in both axes along its entire length from the angle of the mandible to the supraclavicular fossa. In the area of the supraclavicular fossa a coronal image of the junction of the internal jugular and subclavian vein as they unite to form the innominate vein was routinely recorded. The superior vena cava (SVC) was not demonstrated in any patient owing to lack of a suitable acoustic window.

Results

Venography in 22 limbs showed venous patency; however, there was one short-segment subclavian vein stenosis. The remaining eight limbs showed venographic



Figure 2. Digital subtraction angiogram showing a tight stenosis of the subclavian vein. Note this stenosis (arrow) lies directly beneath the clavicle.

evidence of thrombosis. Of these eight cases, six had subclavian vein thrombosis (three in combination with the axillary vein) whilst the remaining two had isolated innominate vein thrombosis. The SVC was visible in only four (50%) of the positive cases and was patent in all. Similarly, the innominate vein was shown in only four cases (50%) and was patent in two cases whilst the other two were thrombosed. The internal jugular vein was not seen in any of the 30 venograms.

Colour Doppler ultrasound was in agreement in all cases with venographically patent central venous systems but missed the one case of subclavian vein stenosis. This false negative scan was because the stenotic segment lay directly underneath the clavicle in an ultrasonic "blind spot" (Fig. 2).

Ultrasound, however, made the primary diagnosis in all eight cases of thrombosis, with the presence of collateral circulation in every case adding confidence to the diagnosis. In addition, the innominate vein was imaged in seven out of eight cases, occlusion being confirmed in five, whilst the internal jugular vein was shown in all eight cases and was occluded in five (see Table I).

Thus in the presence of upper limb thrombosis, ultrasound gives a more complete picture of the local extent of venous involvement although the SVC cannot be shown with this technique.

For axillary and subclavian thrombosis, colour Doppler ultrasound has a sensitivity and specificity of 100%, and an overall sensitivity of 89% and specificity of 100% for occlusion and stenosis combined.

Table 1. Comparison of colour Doppler ultrasound with venography in central vein thrombosis.

	Venography			Colour Doppler ultrasound		
	—	+	NV	—	+	NV
Axillary vein	27	3	0	27	3	0
Subclavian vein	24 (1s)	6	0	24	6	0
Innominate vein	24	2	4	24	5	1
Internal jugular vein	—	—	30	25	5	0
SVC	15	—	4	—	—	19

— patient; + thrombosed; s stenosis; NV = not visualized.

Discussion

The commonest cause of venous thrombosis at the thoracic inlet is central venous catheterization (Drury et al, 1985). Other less common causes include thoracic inlet syndrome, hyperviscosity syndromes and local trauma. To evaluate the accuracy of colour Doppler ultrasound in the diagnosis of upper limb thrombosis we studied a group of 19 renal patients (30 limbs), all of whom had had multiple subclavian lines recently inserted, and compared the findings with venography.

Venography has been the "gold standard" for many years in the diagnosis of veno-occlusive disease. This technique is, however, not without its disadvantages, including unsuccessful venous cannulation in the presence of a swollen limb, and the procedure itself may be painful and distressing to the patient. In addition, there is a small but, nevertheless, real risk of contrast medium reaction as well as the risk of venous toxicity and thrombogenesis (Bettman et al, 1980), although these risks are now less with the introduction of the non-ionic low-osmolar contrast agents (Lea Thomas et al, 1984). In view of this, other less invasive methods have been evaluated in upper limb thrombosis. However, as in lower limb disease they have not been shown to be of sufficient accuracy and reliability for routine imaging (Sottiurai et al, 1982).

B-mode ultrasound with Doppler (duplex ultrasound) has been used to image venous thrombosis in both upper and lower limbs. In the lower limb, the sonographic appearances of venous thrombosis have been well documented, as have the relative advantages of colour Doppler ultrasound (Aitken & Godden, 1987; Cronan et al, 1987; Baxter et al, 1990). In the upper limb, the sonographic appearances and the response of the major veins to various manoeuvres including sniffing and Valsalva have also been well documented (Hightower & Gooding, 1985). Colour Doppler ultrasound is a relatively new technology, but early studies have shown that it may be useful in the follow-up of upper limb thrombosis (Grassi & Polak, 1990).

In our study, colour Doppler ultrasound exhibited spontaneous colour-coded flow, which filled the entire lumen of the vein in all normal venographically patent axillary, subclavian, internal jugular and innominate veins. Although this flow could be retarded by the Valsalva manoeuvre, with accompanying venous distension, or the opposite effect could be achieved by sniffing,

we felt that with the colour demonstration of spontaneous flow these manoeuvres added no additional information.

All patients with occluded subclavian veins showed complete absence of colour-coded flow and the presence of intraluminal echogenic material. In all these cases the subclavian artery was identified confidently and, from the knowledge of the normal anatomical relationship of vein and artery, the diagnosis of an occluded segment of the subclavian vein was made accurately and quickly. In all of the eight positive cases, collateral vessels, undetectable using conventional ultrasound techniques, were identified in the neck giving additional confidence to the diagnosis (Figs 3,4). In five of these eight cases, both the internal jugular (Fig. 5) and innominate vein contained thrombus undetectable using conventional or DSA venographic techniques.

However, colour Doppler ultrasound did miss a short-segment subclavian vein stenosis, of which the

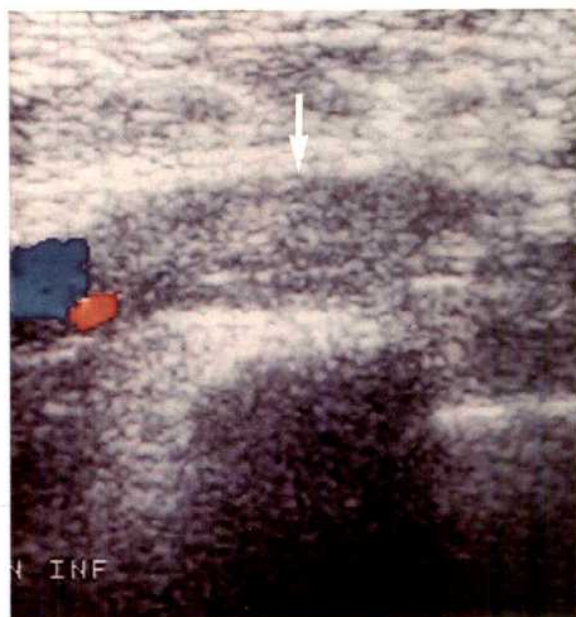


Figure 3. Longitudinal scan showing some turbulent flow in the medial aspect of the axillary vein with complete thrombosis of the subclavian vein (arrow).

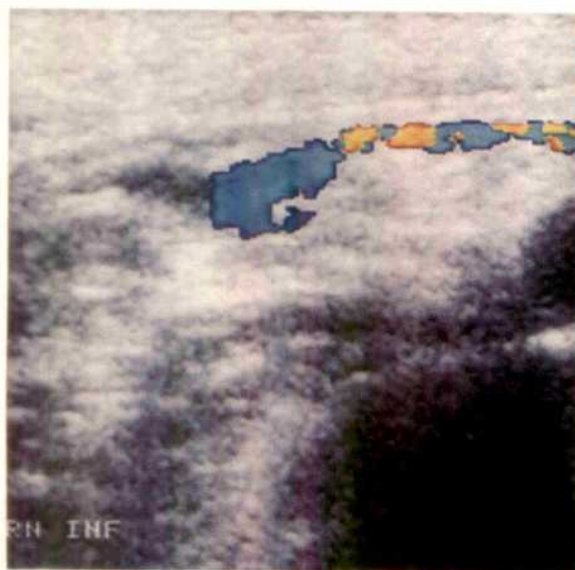


Figure 4. Longitudinal scan in the supraclavicular fossa showing a large collateral vein secondary to subclavian vein thrombosis (same patient as in Fig. 3). This large collateral was also shown by venography.



Figure 5. Supraclavicular transverse scan showing a dilated and thrombosed internal jugular vein (arrow). The common carotid artery lies posteriorly.

Doppler ultrasound features have been documented (Taylor et al, 1987). The reason for the false negative scan on this occasion was undoubtedly due to the anatomical position of the stenosis directly beneath the clavicle. Thus, where clinical features dictate, a venogram should be performed regardless of normal Doppler imaging to exclude stenosis, especially if angioplasty or stenting is a therapeutic option.

In conclusion, these preliminary results suggest that colour Doppler ultrasound is as accurate as venography in the diagnosis of axillary and subclavian vein thrombosis and may give a more complete picture of local involvement by routinely imaging the internal jugular

and innominate veins. Its non-invasive nature, lack of radiation, and financial saving offer certain advantages over venography, whilst the omission of respiratory manoeuvres make it a quicker technique than duplex ultrasound without prejudicing its accuracy.

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The effects of sodium nitroprusside on Doppler signals from a soft tissue tumour

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Abstract. In a previous study, we described the effects of systemic vasoconstriction on the Doppler signals from a soft tissue tumour (Taylor et al, 1989). Our conclusions were that vasoconstriction produced significant changes in the signals from normal vessels and enhanced the differences between normal and neoplastic vessel signals. The aim of this study was to determine whether converse changes were produced by vasodilatation.

Materials and methods

Instrumentation

A 10 MHz continuous wave Doppler system was used. This employed a dual element transducer with a 3 mm diameter face focused 6 mm from the face. Signals were recorded on magnetic tape and subsequently analysed using an Angioscan II spectrum analyser (Unigon) which uses fast Fourier transformation to produce frequency spectra. Each spectrum is of 128 frequency points with a time resolution of 6.5 ms. 512 sequential spectra were fed into an Apple II micro-computer which calculated the maximum frequency shift during systole (MAX), the minimum frequency shift during diastole (MIN), the instantaneous mean frequency, and from this the time averaged mean frequency (TAM). These parameters were derived for each site insonnated and the ratios MAX/TAM and MIN/TAM were calculated. Full details of the instrumentation are described elsewhere (Taylor et al, 1989).

Tumour and insonnation

0.1 ml of a suspension containing cells from a VX2 sarcoma was injected subcutaneously into the left pinna of each of 12 female New Zealand white half-lop cross rabbits. Between 7 and 14 days later the rabbits were sedated intramuscularly with 0.6 ml of Hypnorm (fentanyl citrate 0.315 mg and fluanisone 10 mg/ml). Using calipers, the smallest diameter of the tumour was measured. Doppler recordings were then made at 90° intervals around the circumference of the tumour and from the central artery of the pinna, proximal and distal to the tumour site. An intravenous infusion of sodium nitroprusside 50 µg/kg body weight/min was administered through a vein on the contralateral pinna. A preliminary series of experiments at an infusion rate of 5 µg/kg body weight/min had failed to produce a consistent tachycardia, indicating vasodilatation at that

dose to be insufficient to produce an autonomic response. After 10 min of infusion, the Doppler recordings were repeated. All experiments were conducted in the same air conditioned room at an ambient temperature of 16-18°C.

Results

The results are shown in Table I and Figures 1 and 2. All rabbits experienced a rise in heart rate during the infusion. The MIN/TAM ratio fell in all but two of the tumours and a fall was also observed in 13 of the 20 arterial sites. When the pre- and post-vasodilated ratios were compared, there was no statistically significant difference between them (Student's *t*-test). With respect to the MAX/TAM ratio, seven of the tumours showed a rise but no statistically significant difference could be demonstrated between the basal and vasodilated signals. A rise in the MAX/TAM ratio was seen in all but four of the arterial sites and, where a fall was observed, it was small in magnitude. A significant ($p < 0.02$) difference was observed between the MAX/TAM ratios from the basal and vasodilated arteries.

Discussion

Previous studies have demonstrated Doppler blood flow signals arising from malignant tumours and the surrounding vasculature (Mountford & Atkinson, 1979; Burns et al, 1982; Dubbins & Wells, 1986). Recent studies have suggested that in addition to detecting lesions, Doppler studies may be of value in tissue characterization (Ramos et al, 1988; Kuijpers & Jaspers, 1989). We have studied previously the VX2 sarcoma and demonstrated that the signals can be manipulated pharmacologically by the use of a vasoconstrictor (Taylor et al, 1989). We concluded that the MIN/TAM ratio could be used to differentiate tumour and arterial signals in both the basal and the vasoconstricted state. The MAX/TAM ratio, although not helpful in differentiating the two sources in the basal state, could be used

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Table 1. The age and size of tumours and the calculated MAX/TAM and MIN/TAM ratios for the tumour and arterial sites, before and after sodium nitroprusside

Rabbit	Tumour age (days)	Size (mm)	MAX/TAM					
			Tumour		Artery proximal		Artery distal	
			Pre	Post	Pre	Post	Pre	Post
1	10	12	4.00	4.06	3.63	3.51	3.42	3.83
2	10	15	4.09	3.49	2.75	2.94	2.70	2.75
3	8	12	3.83	3.91	2.85	4.53	2.80	4.36
4	8	9	3.60	4.22	2.79	2.73	2.89	2.80
5	7	14	3.65	3.40	2.79	2.91	3.14	3.03
6	7	7	3.59	4.34	2.93	3.82	2.91	4.35
7	10	13	3.62	3.59	3.18	4.05	2.91	3.43
8	9	9	3.62	4.85	2.72	2.77	2.94	2.90
9	9	11	4.25	6.14	2.95	4.44	3.74	5.20
10	11	14	4.46	4.40	3.16	3.16	3.49	3.58

Rabbit	Tumour age (days)	Size (mm)	MIN/TAM					
			Tumour		Artery proximal		Artery distal	
			Pre	Post	Pre	Post	Pre	Post
1	10	12	2.18	2.03	1.54	1.50	1.61	1.31
2	10	15	2.06	1.97	1.63	1.78	1.58	1.64
3	8	12	2.65	2.23	1.70	1.40	1.75	1.45
4	8	9	2.50	2.46	1.68	1.56	1.60	1.58
5	7	14	2.02	2.05	1.51	1.70	1.48	1.71
6	7	7	1.94	1.77	1.38	1.27	1.41	1.15
7	10	13	1.93	1.89	1.49	1.36	1.53	1.39
8	9	9	2.03	2.31	1.73	1.61	1.84	1.72
9	9	11	1.92	1.79	1.46	1.10	1.59	1.71
10	11	14	2.17	1.91	1.58	1.58	1.69	1.55

following vasoconstriction owing to a significant fall in this ratio from the arterial signals. The aims of this study were to assess whether the converse, a rise in the MAX/TAM ratio, occurred, to assess its magnitude and to observe whether any changes occurred to the MIN/TAM ratio.

Sodium nitroprusside is a potent vasodilator, acting on both arterial and venous blood vessels. It acts directly on the vascular musculature and vasodilatation is independent of the autonomic nervous system. In humans it is used in the treatment of hypertensive crises but its use is restricted, since it can produce severe hypotension; it is metabolized to form the potentially toxic thiocyanate and there is a wide variation in patient tolerance. Recommended infusion rates range from 0.5 to 8 µg/kg body weight/min (Bowman & Rand, 1980). The absence of a direct autonomic action means that reflex tachycardia can be used as an indirect physiological measurement of the degree of vasodilatation. This was used to establish the rate of infusion (50 µg/kg body weight/min).

It was postulated that vasodilatation, decreasing both venous and arterial resistance, resulting in an increased flow rate, would produce a decrease in time averaged mean flow velocity within the dilated vessels. The maxi-

mum and minimum velocities are difficult to predict since they are multifactorial, depending on factors arising from the blood vessels (*e.g.* wall compliance), the blood (*e.g.* viscosity) and remote factors (*e.g.* cardiac rate). Since tumours and normal vessels would both be subject to any changes in blood composition or remote factors it is postulated that any observed changes in the flow parameters are the result of changes in the vessels themselves. The signals arising from the tumour originate from both resistive and capacitive vessels, which are immature and lack contractile elements (Lagergren *et al.*, 1960). The responses of the tumour vessels are therefore variable.

These hypotheses are supported by the results. The only significant changes were observed in the MAX/TAM ratio of the arterial signals. Overall, these demonstrate a significant rise, supporting either a fall in the time averaged mean or a rise in the maximum velocity. The MAX/TAM ratio from the tumour showed a general but inconsistent rise. Our previous study had shown an overlap in the MAX/TAM ratios between the tumour and artery in the basal state. This was observed again and the overlap became greater following vasodilatation.

We had suggested previously that a MIN/TAM ratio

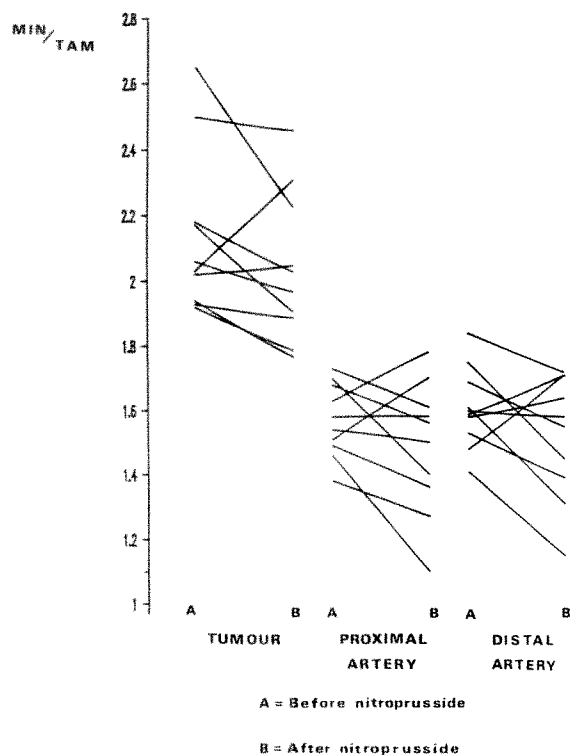


Figure 1. MIN/TAM ratio before and after vasodilation in the tumour and the central artery proximal and distal to the tumour.

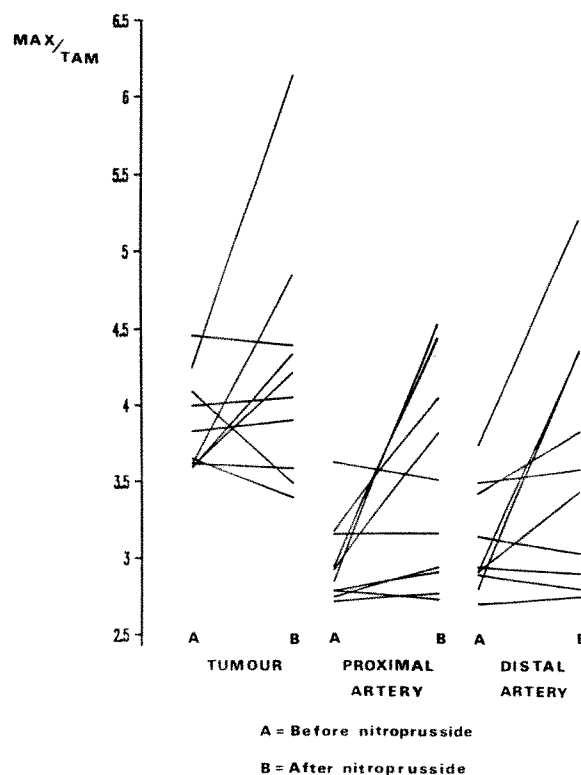


Figure 2. MAX/TAM ratio before and after vasodilation in the tumour and the central artery proximal and distal to the tumour.

>1.8 arose exclusively from a tumour source. The present results would support this; 19 of the 20 arterial sources having a lower ratio in the basal state. Following vasodilation, two of the tumours produced ratios <1.8 (1.77 and 1.79). Despite this there is little overlap between the MIN/TAM ratios of the tumour and arterial sources; the ratio remaining a reliable parameter in differentiating the sites.

Our conclusions are that vasodilation with nitroprusside produces a significant rise in the arterial MAX/TAM ratio, but no significant change in the MIN/TAM ratios of either the tumour or the arterial signals. The significance of these observations is that the MIN/TAM ratio can differentiate the two sources in the basal, the vasoconstricted and the vasodilated subjects. Although the MAX/TAM ratio has been shown previously to differentiate the sources in the vasoconstricted state, during vasodilation significant overlap between the two sources occurs. If these results are applied to other tumours, particularly in humans, they emphasize the importance of correct parameter selection. The vascular tone of the subject should be considered, vasodilation and vasoconstriction both altering the derived parameters.

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Duplex ultrasound of the common femoral vein in pregnancy and puerperium

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Abstract. The common femoral veins of 34 apparently normal women were examined by ultrasound during or just after pregnancy. The cross sectional areas of these veins were measured at rest in the supine position and during a Valsalva manoeuvre. The veins were also assessed by pulsed Doppler ultrasound. We believe that Doppler examination is superior to calibre response assessment during the Valsalva manoeuvre in excluding an isolated iliac occlusion in women in late pregnancy and in early puerperium.

Fatal pulmonary embolus occurs in 1:100 000 pregnancies in this country and it vies with hypertensive disease of pregnancy as the commonest cause of maternal death. The most recent *Report on Confidential Enquiries into Maternal Deaths in England and Wales* (Turnbull et al, 1989) calls for earlier detection of thrombus in the veins of the pelvis and legs, and states that reduced flow in the femoral vein detected by non-invasive methods is an indication for anticoagulant therapy.

The incidence of deep vein thrombosis (DVT) is around 0.6 per 1000 pregnancies in both the antenatal and postnatal periods. (Bergqvist et al, 1983a; Kierkegaard, 1983; Polak & O'Leary, 1988). DVT in pregnancy more frequently originates in the iliofemoral segment rather than in the calf veins (Bergqvist et al, 1983a; Bergqvist & Hedner, 1983b). This is distinct from the non-obstetric DVT which tends to originate distally. Furthermore, of those thromboses which result in fatal pulmonary embolus, over half are confined to the iliac veins (Turnbull et al, 1989). This presents problems in diagnosis. The clinical features are atypical often with lower abdominal or pelvic pain and oedema. Unlike the distal veins, the iliac veins are inaccessible to compression ultrasound.

Cuff impedance plethysmography and phleboreography are not widely practised in the UK and false positive results have been reported during pregnancy (Clarke-Pearson & Jelovsek, 1981; Nicholas et al, 1985).

Ultrasound

Frede and Ruthberg (1988) used the gravid uterus of 25 weeks' gestation as an acoustic window to image the iliac veins directly (Fig. 1) and demonstrate a thrombo-



Figure 1. Sonogram of the iliac vessels through a 16 week gestation gravid uterus as an acoustic window. CIV = common iliac vein, CIA = common iliac artery, IIA = internal iliac artery, EIA = external iliac artery.

sis. This method relies on imaging echogenic thrombus and would not detect fresh thrombus which is often isoechoic with blood. Furthermore, isolated iliac DVT is more frequent in late pregnancy when the iliac veins are often outside the focal zone of most probes.

The increase in calibre of the common femoral vein (CFV) during the Valsalva manoeuvre has been used to assess the patency of the iliofemoral segment (Effeney et al, 1984). A 50% or more increase in antero-posterior (AP) diameter is quoted as a criterion for patency and a 10% or less increase as a criterion for occlusion. This indirect method of assessing the iliac veins has been used by other authors (Appleman et al, 1987; O'Leary & Kane, 1988; Zwiebel, 1988) and its use has been

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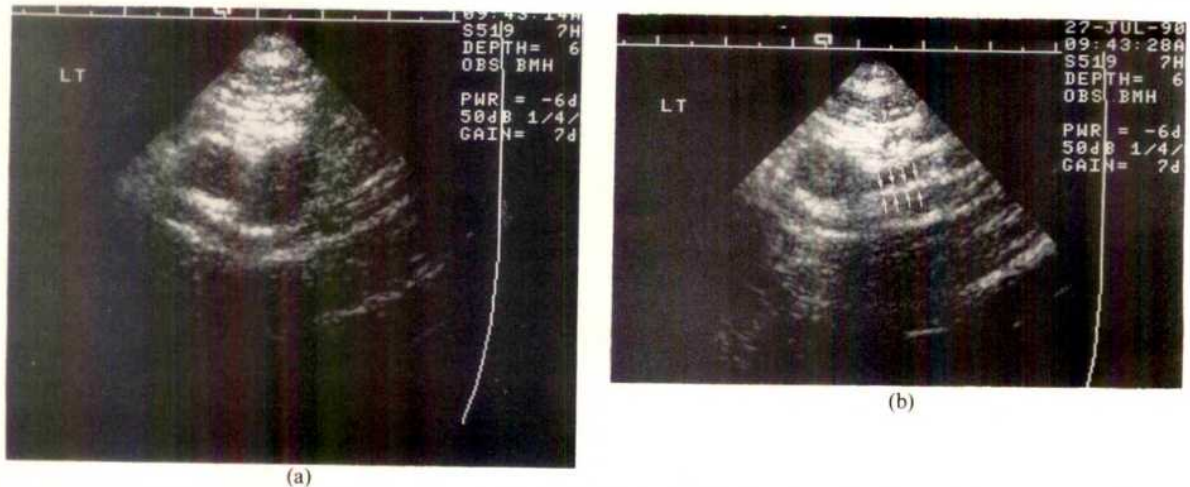


Figure 2. Transverse sonogram of the common femoral vessels (a) at rest and (b) during compression with the transducer. There is complete collapse of the CFV during compression (arrows).

advocated in suspected DVT during pregnancy (Polak & O'Leary, 1988).

Pulsed Doppler sampling of the CFV offers a further indirect method of assessing iliac vein patency (O'Leary & Kane, 1983; Thiele, 1984; Zwiebel, 1988). The Doppler signal from the CFV should be spontaneous, phasic and unidirectional. Lack of spontaneous flow implies occlusion at, proximal to or distal to the CFV. Lack of respiratory phasic variation of the signal (caused by pressure changes in response to the respiratory cycle) implies occlusion proximal to the CFV. Retrograde flow in the CFV implies valvular incompetence.

Venous flow may be augmented by compression of veins distal to the sample site or by the release of a compression proximal to the sample site (Thiele, 1984).

Although compression proximal to the CFV may not be possible directly, the Valsalva manoeuvre (by increasing intra-abdominal pressure) has a similar effect. There is complete cessation of flow followed by augmentation as normal respiration is resumed, provided the iliac veins are patent. Iliac occlusion abolishes this Valsalva response of the Doppler signal.

Augmentation by distal compression is abolished by occlusion distal to the sample site, but according to Thiele (1984) remains intact in the presence of a proximal occlusion. O'Leary & Kane (1988), on the other hand, suggest that loss of augmentation at the CFV with calf compression may indicate an iliac vein occlusion. Pulsatile flow in the extremities is said always to be abnormal and usually caused by congestive heart failure (Zwiebel, 1988).

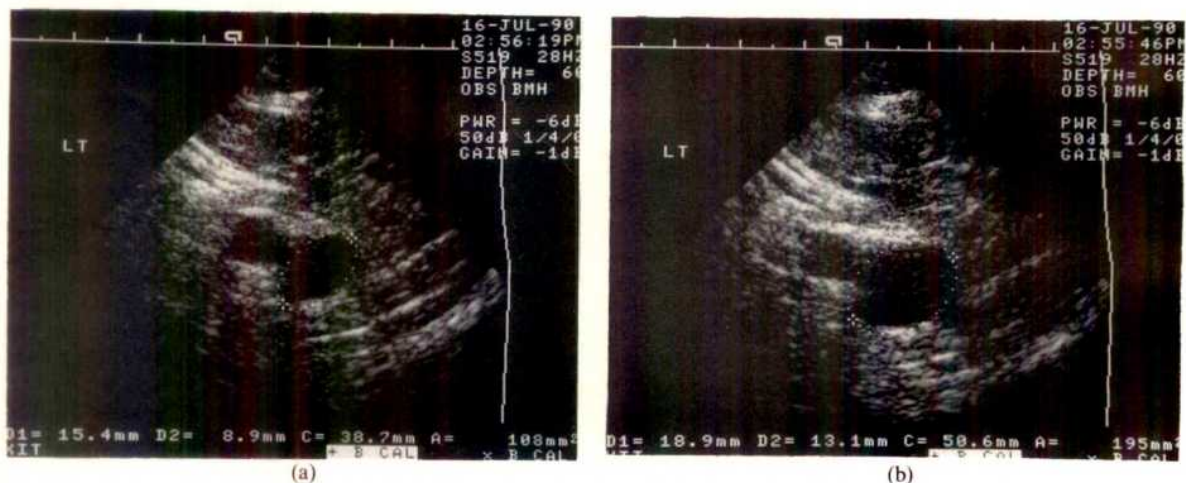


Figure 3. Transverse sonogram of the CFV (a) at rest and (b) during a Valsalva manoeuvre. D_1 = major axis, D_2 = minor axis, A = cross sectional area.

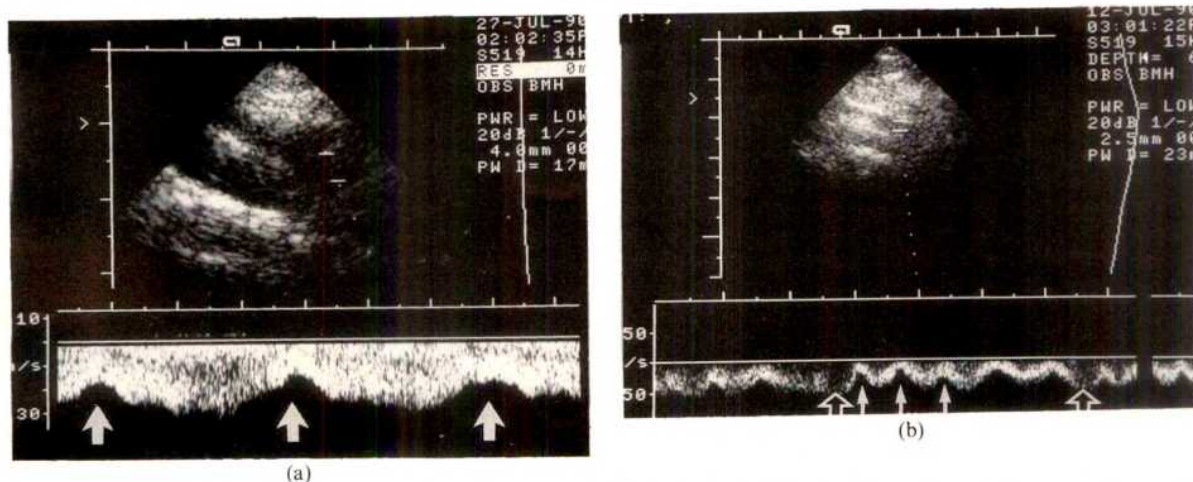


Figure 4. Pulsed Doppler scan of the CFV showing spontaneous flow. (a) Flow is phasic with the respiratory cycle (arrows). (b) Pulsatile flow with the cardiac cycle (arrows) is superimposed on respiratory phasic variation (open arrows) in a patient with no history or signs of heart disease.

The aim of this study was to determine the effect of the enlarged uterus in late pregnancy and early puerperium on the Doppler characteristics of the CFV and on the Doppler and calibre response of the CFV to the Valsalva manoeuvre.

Patients and method

Ultrasound assessment was made of 68 CFVs in 34 women. 10 were in early pregnancy (8 to 9 weeks' gestation). 19 women were in late pregnancy (28 to 40 weeks' gestation) one of whom was carrying twins at 37 weeks. Five women were between 2 and 10 days post-partum, two of whom had been delivered by caesarian section. All the women were normal volunteers with no clinical evidence of DVT. None of the women were examined more than once.

Real-time ultrasound was performed using an electronically focused 5 MHz sector transducer with 5 MHz pulsed Doppler capability (Acuson, Mountain View, California). The lowest possible high pass filter (125 Hz)

was selected. The women were examined in the supine position. The CFVs were imaged transversely and longitudinally and assessed for their compressibility and the presence of intraluminal echoes (Fig. 2). The veins were examined at the level just proximal to the bifurcation of the common iliac artery.

Assuming an elliptical cross section, the major and minor axes were measured and the cross sectional area calculated. The area is produced automatically by our machine, but can be calculated using the equation: $\text{area} = \frac{\pi}{4} \times \text{major axis} \times \text{minor axis}$. Area measurements were performed at rest and during a Valsalva manoeuvre (Fig. 3).

Pulsed Doppler assessment was made during quiet respiration to elicit respiratory phasic variation of the signal (Fig. 4a). The women were then asked to perform the Valsalva manoeuvre and the Doppler signal was assessed to determine whether blood flow was blocked (*i.e.* reduced below the level of the high pass filter), merely reduced but still detectable, or whether flow was

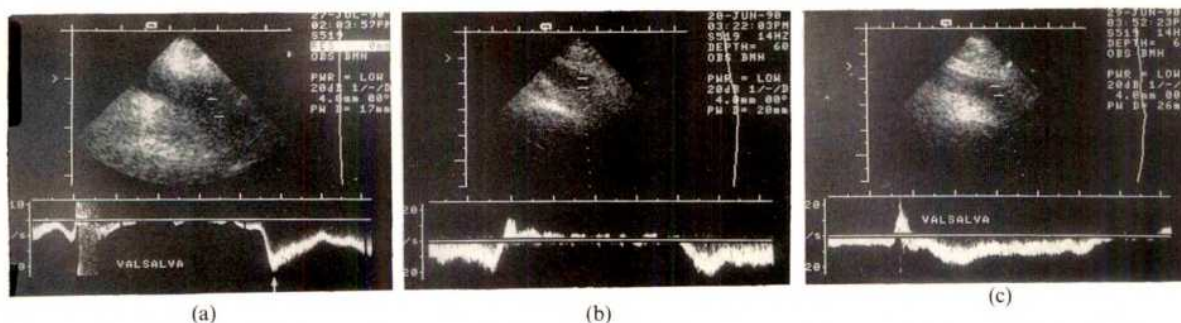


Figure 5. Pulsed Doppler scan showing the CFV flow response to a Valsalva manoeuvre. (a) Complete block is achieved. There is augmentation of flow as normal breathing is resumed (arrow). (b) Reversed flow is achieved implying incompetence of venous valves. (c) Increased antegrade flow during a Valsalva manoeuvre at 39 weeks' gestation. This would seem to be a spurious response to an incorrectly performed Valsalva.

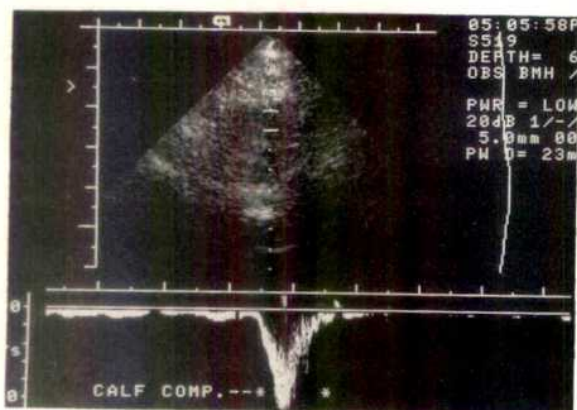


Figure 6. Pulsed Doppler scan showing normal augmentation of CFV flow during calf compression.

reversed (Fig. 5). As normal respiration was resumed the presence of post Valsalva accentuation of the signal (proximal augmentation) was recorded. Finally, the presence of accentuation of the signal due to digital compression of the calf (distal augmentation) was assessed (Fig. 6).

Seven CFVs in four women in their third trimester of pregnancy were also examined in the opposite decubitus positions, *i.e.* the vein under examination being uppermost. A *t*-test on a logarithmic transformation of the data was used to compare the means for two-sided *p* values.

Results

Of the 68 CFVs examined, all were easily compressible and there would have been no difficulty in excluding CFV thrombosis. No intraluminal echoes were found in the veins examined in the first trimester group. Moving echoes were seen in 16/38 (42%) of veins in the third trimester and in 2/10 (20%) of veins in the postnatal group. Static intraluminal echoes were found in none of the veins examined.

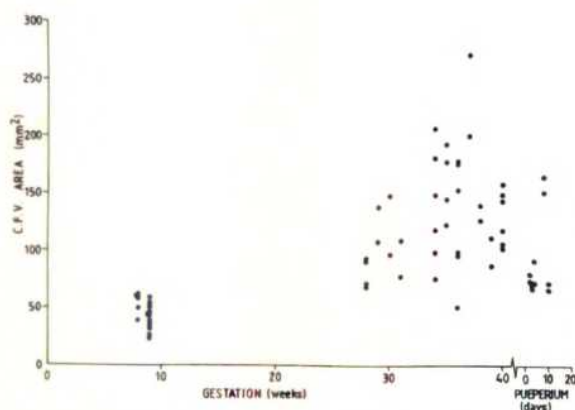


Figure 7. Resting CFV cross sectional area plotted against gestational age and number of days post-partum.

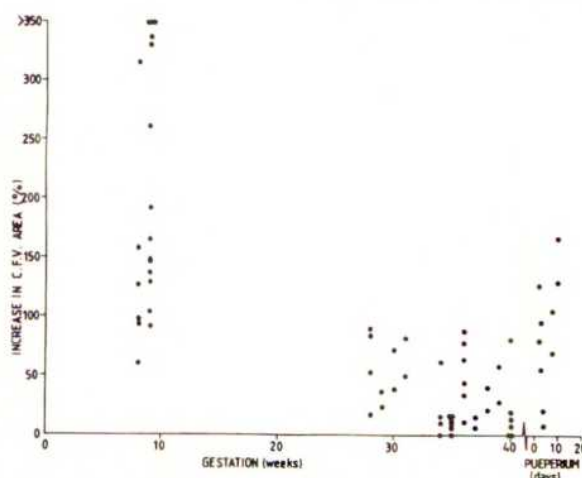


Figure 8. Percentage increase in CFV cross sectional area during a Valsalva manoeuvre plotted against gestational age and number of days post-partum.

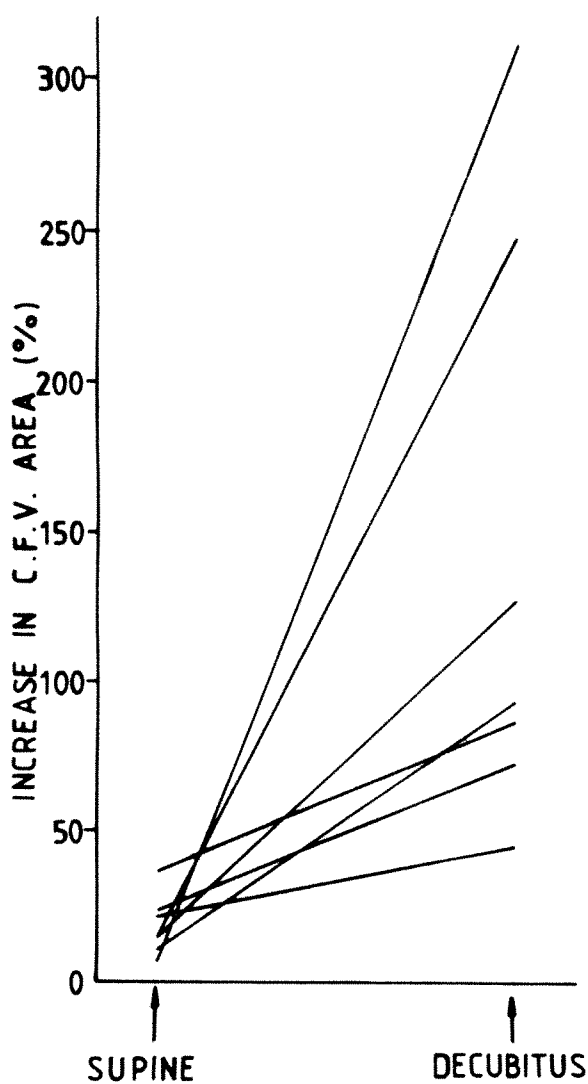
In Figure 7 the CFV cross sectional area is plotted against gestational age and number of days post-partum. In Figure 8 the percentage increase of CFV cross sectional area during a Valsalva manoeuvre is plotted similarly. The mean resting cross sectional areas and the mean percentage increase in areas during a Valsalva manoeuvre between the three groups and between the right and left sides are summarized in Table I. There was no significant difference between the sizes of the right and left CFVs in any of the three groups. The mean cross sectional area of the CFVs in the third trimester group (130.1 mm^2) and in the post-partum group (91.0 mm^2) were significantly greater ($p < 0.001$ and $p < 0.001$, respectively) than in the first trimester group (45.6 mm^2). Similarly, the mean percentage increase in areas during a Valsalva manoeuvre in the third trimester (34.5%) and the post-partum groups (86.2%) were significantly lower ($p < 0.001$ and $p < 0.001$, respectively) than in the first trimester group (203.8%).

Seven veins of women in the third trimester were also examined in the opposite decubitus position and the CFV assessed. This reduced the mean cross sectional area at rest from 173.0 mm^2 (supine) to 92.1 mm^2 . The effect of this on the percentage increase in cross sectional area during a Valsalva manoeuvre is shown in Figure 9. The mean percentage increase (supine) at 18.3% was increased to 140.7% (decubitus).

Spontaneous antegrade flow was elicited in all CFVs examined by pulsed Doppler. Phasic variation with respiration (Fig. 4a) was present in all veins in the first trimester and postnatal groups and in 92% of veins in the third trimester group, flow being continuous in three veins. Of these, there was a normal Doppler response to a Valsalva manoeuvre, *i.e.* complete block plus post Valsalva augmentation (Fig. 5a) in two and increased antegrade flow on the Valsalva in the third (Fig. 5c). Cardiac pulsation was superimposed on the respiratory

Table 1. Results of cross sectional area assessments of the common femoral veins

		Cross sectional area (mm ²)		Percentage increase in area on a Valsalva manoeuvre (%)	
		At rest	On a Valsalva manoeuvre		
		Mean	(SD)	Mean	(SD)
First trimester <i>n</i> = 20	Right	45.9	(20.3)	135.2	192.2 (98.7)
	Left	45.4	(12.0)	130.4	215.4 (121.7)
	Total	45.6	(16.4)	132.8	203.8 (110.8)
Third trimester <i>n</i> = 38	Right	129.0	(42.1)	163.6	31.8 (28.8)
	Left	130.9	(49.4)	170.1	36.9 (28.1)
	Total	130.1	(45.5)	166.8	34.4 (28.6)
Post-partum <i>n</i> = 10	Right	89.8	(37.7)	171.4	96.2 (49.6)
	Left	92.2	(31.1)	164.0	76.2 (41.8)
	Total	91.0	(34.6)	167.7	86.2 (46.9)



undulation of the signal in the veins of two patients (Fig. 4b), one in the first and one in the third trimester. Neither of these women had a history or signs of heart disease.

Retrograde flow on the Valsalva manoeuvre was detected in five veins (13%) in the third trimester group (Fig. 5b). A Valsalva response comprising complete block or retrograde flow plus post Valsalva augmentation was present in 90% in the first trimester, 50% in the third and 60% in the postnatal group.

One woman at 39 weeks' gestation produced an increase in antegrade flow in both CFVs during the Valsalva manoeuvre (Fig. 5c). The same manoeuvre produced 58% and 28% increases in the cross sectional areas of the right and left CFVs, respectively. There was no augmentation on cessation of the Valsalva (only during the Valsalva). Flow in the right CFV at rest was non-phasic in this patient.

Of the seven veins examined in the decubitus position, phasic variation was more pronounced than in the supine position in four and a normal Doppler Valsalva response was obtained in five veins where it had been normal in only two in the supine position. All patients had positive, normal distal augmentation (Fig. 6).

Discussion

The CFV at rest is approximately elliptical in cross section. The orientation of the major axis of the ellipse is variable and not always parallel to the skin surface. During deep inspiration and a Valsalva manoeuvre the CFV enlarges and usually becomes more circular in cross section, *i.e.* the minor axis increases more than the major axis. This, however, is not always the case. There was a proportionally greater increase in the major axis on a Valsalva manoeuvre in 30% of CFVs in our first trimester group and in 44% in the third trimester. For

Figure 9. The effect, of examining in the decubitus position, on the percentage increase in cross sectional area during a Valsalva manoeuvre in late pregnancy.

Table II. Results of pulsed Doppler assessments of the common femoral veins

	First trimester		Third trimester		Post-partum	
	n = 20	(%)	n = 38	(%)	n = 10	(%)
Spontaneous	20	(100)	38	(100)	10	(100)
Phasic	20	(100)	35	(92)	10	(100)
Pulsatile	2	(10)	2	(5)	0	
Valsalva response						
Complete block	19	(95)	16	(42)	8	(80)
Decreased flow	1	(5)	15	(40)	2	(20)
Reversed flow	0		5	(13)	0	
Increased flow	0		2	(5)	0	
Post Valsalva augmentation	19	(95)	27	(71)	6	(60)
Calf compression augmentation	20	(100)	38	(100)	10	(100)

these reasons we chose to measure the minor and major axes and calculate the cross section area of the CFVs, rather than measure the AP diameter.

Effeney et al (1984) concluded that a 50% (1.5 fold) increase in diameter of the CFV during a Valsalva manoeuvre indicated patency and that an increase of 10% (1.1 fold) or less was suggestive of iliac occlusion. The range 10–50% being equivocal or indeterminate. Assuming that the cross sectional area is approximately proportional to the square of the AP diameter, then a 10% increase in diameter would correspond to a 21% increase in area as $(1.1 \text{ fold})^2 = 1.21 \text{ fold}$. A 50% increase in diameter would correspond to a 125% increase in area as $(1.5 \text{ fold})^2 = 2.25 \text{ fold}$.

Of the 20 CFVs examined in the first trimester, five (25%) fell into the 21–125% indeterminate range and 15 (75%) were above 125%, *i.e.* true negatives. Of the 38 CFVs examined in the third trimester all increased in area by less than 125% during a Valsalva manoeuvre. Assuming that our volunteers were normal and that the criteria for normality and abnormality are correct, then by this method there were no true negatives in this group. Moreover, 19 veins fell in the abnormal range of 21% or less, *i.e.* 50% were falsely positive, and of those examined after 34 weeks' gestation, 64% were falsely positive. This situation was improved somewhat in those veins which were examined in the decubitus position (Fig. 9). Three veins which, in the supine position were in the abnormal range of 21% or less, were moved into the normal range of 125% or more when the resting cross sectional area was measured in the decubitus position. The other four veins were merely moved into or higher up the indeterminate range.

In the postnatal group the veins of one patient fell into the abnormal range. However, being only 4 days post-caesarian section she found difficulty in performing an adequate Valsalva manoeuvre. This was reflected in the Doppler analysis which showed only a modest decrease in flow during the Valsalva. Five other veins in the group (50%) were indeterminate and only three (30%) were in the normal range.

Where changes in calibre reflect pressure changes, Doppler frequencies reflect blood flow. Blood flow would appear to be less influenced by the presence of a gravid uterus with normal spontaneous phasic flow being present in 92% of veins in the third trimester even in the supine position. The presence of sustained reversed flow during the Valsalva manoeuvre in 13% of the veins in the third trimester group would suggest that the dilatation which occurs in late pregnancy renders a proportion of normal venous valves incompetent. Reversed flow was not detected in the other groups. The increase in antegrade flow during the Valsalva manoeuvre in one patient is difficult to explain (Fig. 5c). Most likely it was caused by incorrect performance of the Valsalva manoeuvre, *e.g.* attempted inspiration against the closed glottis rather than attempted expiration, thus reducing intrathoracic pressure and increasing venous return.

The clinical implications of making a diagnosis of venous thrombosis in pregnancy are considerable. The risks of fatal pulmonary embolus have already been outlined. The use of oral anticoagulant treatment is limited by the teratogenic effects in the first trimester and the risks of fetal haemorrhage during labour. Although heparin does not cross into the fetal circulation its use is also not without hazard. The use of oral anticoagulants in the puerperium denies the option of breast feeding. Women with thrombosis which is resistant to anticoagulant treatment, particularly those with recurrent pulmonary emboli, may be considered for the placement of a caval filter.

Compression ultrasound of the femoral and popliteal veins continues to be the first investigation for suspected DVT in pregnancy. This should pick up the majority of cases where these segments are involved. Doppler assessment of the CFV should be used to exclude iliac thrombosis in women with a normal femoropopliteal segment. Iliac venography should be reserved for women where there is poor correlation between clinical suspicion and Doppler finding and where placement of a caval filter is contemplated.

Conclusion

The calibre response of the CFV to a Valsalva manoeuvre in the supine position in women in late pregnancy and early puerperium is unreliable. Examination in the decubitus position may be more likely to exclude an iliac vein occlusion.

We believe that Doppler assessment of the CFV is superior to the measurement of calibre changes in excluding iliac thrombosis in obstetric patients. If Doppler assessment is abnormal or equivocal then the patient should be examined in the decubitus position.

In pregnancy pulsatile flow in the CFV may be present in the absence of cardiac disease, and in late pregnancy retrograde flow during a Valsalva manoeuvre may be present in the absence of diseased venous valves.

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The use of real-time ultrasound in the management of scrotal trauma

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Keywords: Ultrasound, Scrotal trauma

Abstract. 27 patients were studied with real-time ultrasound following severe scrotal trauma. 22 (81.5%) had ultrasound features of scrotal trauma and, of these, five (18.5%) had signs of testicular rupture. Four of these five patients underwent surgery following ultrasound. This confirmed the diagnosis of rupture and the testes were repaired. Ultrasound should be offered to all patients presenting with scrotal trauma to select patients with testicular rupture for surgery.

Scrotal trauma of sufficient severity for the patient to present to hospital is unusual. Of these only about 20% will have sustained testicular rupture (Anderson et al, 1983; Lupetin et al, 1983). Most scrotal injuries present with the clinical triad of pain, tenderness and swelling (Schaffer, 1985). It is often impossible to distinguish testicular rupture clinically from less severe scrotal injuries (Jeffrey et al, 1983). The distinction is of importance as early operative intervention dramatically improves the chances of salvaging a ruptured testis (Gross, 1969). Less severe scrotal injuries may be managed conservatively (Anderson et al, 1983; Schaffer, 1985). Our experience shows that scrotal ultrasound examination can reliably differentiate between testicular rupture and other less severe scrotal injuries and, therefore, help in the selection of patients who may benefit from early surgery.

27 patients who presented to our institution following blunt scrotal trauma between 1983 and 1989 were studied. There was a wide age range (5-68 years) but in fact all but three patients were aged between 16 and 37 years. Most injuries (74%) were from a kick sustained during a fight.

Methods

Scans were performed on the day of request or on the next day if the patient presented during the night. Unfortunately there was often some delay between the injury and the patient presenting to hospital. Although most scans were performed within the first few days after injury, nine scans (33%) were performed more than 1 week after injury (maximum delay 2 months). Early in the study a low frequency (3.5 MHz) probe was used (nine scans), but all recent scans were performed with a high frequency probe (four scans with 5 MHz, 14 scans with 7.5 MHz). Despite pain and tenderness we were able to obtain good quality images in all patients.

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Results

The results are shown in Table I. Less than 20% of the scans performed were normal but only one patient had bilateral injuries.

Loss of the testicular outline was the consistent finding in the five patients with testicular rupture. In four of these patients the testicular parenchymal reflectivity was abnormal, presumably owing to associated contusion (Fig. 1a). A fracture plane through the testis was seen in only one case (Fig. 1b). In three of the five cases there was an associated collection of blood.

As a result of the ultrasound diagnosis, four of the five patients with testicular rupture underwent surgery. In one patient there was complete internal disruption of the testis so a subcapsular orchidectomy was performed. Histology revealed a seminoma not previously suspected, neither clinically nor on ultrasound (Fig. 2). Following more radical local surgery this patient remains disease free 2 years later. In three further patients, viable testicular tissue was replaced within the tunica albuginea which was repaired. The fifth patient

Table I. Ultrasound findings

Ultrasound findings	No. of patients	Additional pathology
Rupture	5	Haematoma 2
Contusion	5	Haematoma 2
		Haematocoele 2
		Epididymitis 2
Haematoma	7	
Haematocoele	2	
Traumatic epididymitis	2	
Atrophy	1	
Normal	5	
Total	27	

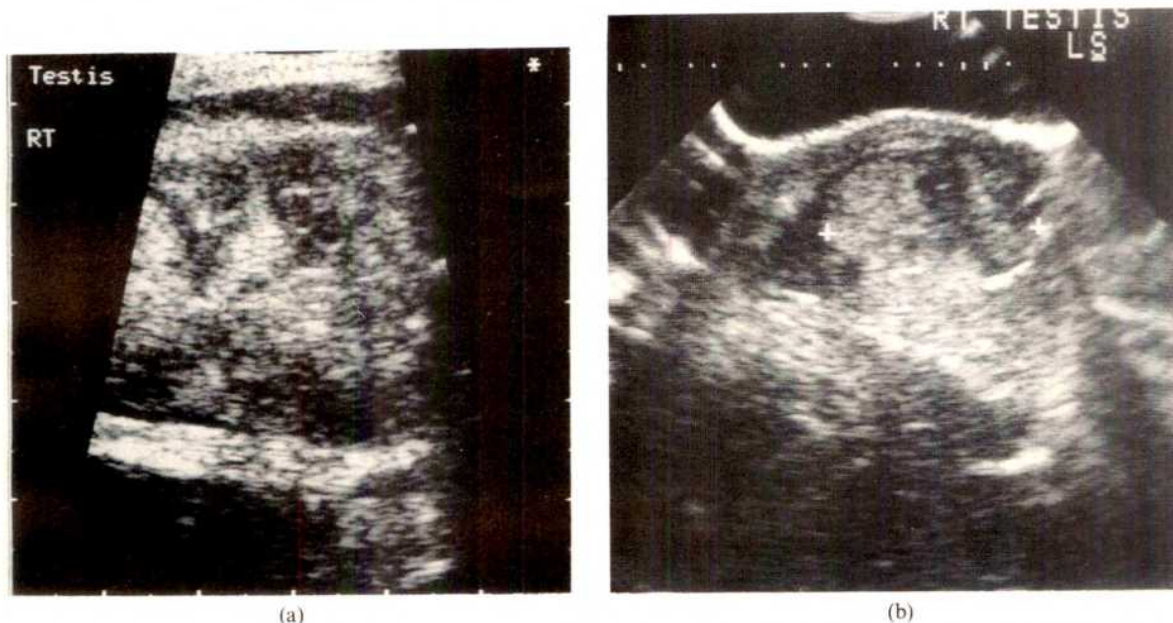


Figure 1. (a) Testicular rupture. There is loss of the testicular outline with diffusely abnormal parenchymal reflectivity. (b) Testicular rupture: there is loss of the testicular outline with a fracture plane through the testis.

did not undergo surgery and was unfortunately lost to follow-up.

In the five patients with testicular contusion the testicular reflectivity was either decreased or increased. The testicular outline remained intact.

The appearance of extratesticular haemorrhage varies depending on the age, size and site of the blood. A haematoma usually lies within the scrotal wall whereas a hydrocoele lies between the layers of the tunica vaginalis

(Hricak & Filly, 1983). Haematoma was easily the commonest abnormality observed occurring in 11 patients, including 4 with other types of scrotal injury (Figs 3 & 4). Figures 5 and 6 demonstrate the ultrasound features of interest in two of the four patients with a haematocoele.



Figure 2. Testicular rupture and seminoma. There is a diffusely abnormal, heterogeneous parenchymal reflectivity.



Figure 3. Localized haematoma. There is an echo-poor collection lying adjacent to a normal testis.



Figure 4. Chronic haematoma. There is a 10 cm diameter, homogeneous solid mass filling one scrotum. (This patient presented with scrotal enlargement but no history of trauma.) Surgery unexpectedly revealed a chronic haematoma.

With the exception of the patient with a chronic haematoma presenting as scrotal enlargement (Fig. 4), all the patients with injuries other than rupture were successfully and conservatively treated.

Discussion

Our results show a distribution of types of injury similar to those documented in previously reported series (Anderson et al, 1983; Jeffrey et al, 1983; Lupetin et al, 1983).



Figure 5. Early haematocoele. Note the fluid collection surrounding the testis — the few low level echoes within the fluid distinguish this from a hydrocoele.



Figure 6. Chronic haematocoele. There is a large complex multiseptate collection surrounding the testis.

Surgical repair of testicular rupture within 72 h of injury improves testicular salvage rate from 30% when performed after 72 h to over 80% (Gross, 1969). Prompt diagnosis and treatment is, therefore, essential.

Some authors, aware of the clinical difficulties in distinguishing testicular rupture from less serious injuries, have advocated surgical exploration whenever there is a clinical possibility of testicular rupture (Gross, 1969). However, the demonstration of scrotal contents using ultrasound, a quick and non-invasive procedure, allows not only accurate diagnosis of testicular rupture (Albert, 1980; Anderson et al, 1983; Jeffrey et al, 1983; Lupetin et al, 1983; Schaffer, 1985), but selection of those patients who may benefit from early surgery.

The incidental finding of a seminoma in one patient underlines the importance of considering possible additional or underlying disease. Conversely, a chronic haematoma may present as a solid scrotal mass with no history of trauma and be indistinguishable from a tumour both clinically and on ultrasound.

Conclusion

It is possible with care to obtain diagnostic images with ultrasound in patients who have suffered severe scrotal trauma. We believe ultrasound examination should be offered to all such patients — most scans will be abnormal and will allow a more rational choice between surgical and conservative management than is possible on clinical findings.

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The use of real-time ultrasound in the management of scrotal trauma

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Air aspiration after double-contrast knee arthrography: a worthwhile exercise?

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Keywords: Double-contrast knee arthrography, Air aspiration

Abstract. A prospective study following double-contrast knee arthrography was undertaken to compare pain and discomfort experienced at the conclusion of the procedure and for 7 days afterwards. The patients were divided into two groups. Half had the air aspirated at the end of the examination and the other half did not. Twice as many patients in the aspirated group were totally asymptomatic (48% compared with 22%); however, by 7 days after the procedure the numbers of asymptomatic patients were similar in the two groups (64% and 63%, respectively). Thus our conclusion is that air aspiration after double-contrast knee arthrography does reduce short-term morbidity.

The technical aspects of double-knee arthrography have been well discussed (Butt & McIntyre, 1969; Freiburger & Puvlov, 1988), but there is only anecdotal evidence as to whether aspiration of air results in reduced morbidity. Pain and discomfort is a common complaint for 48 h after the procedure, and some advocate air aspiration at the end of the procedure in an attempt to reduce this complication (Arndt et al, 1981). The object of this study is to assess whether the practice of air aspiration is worthwhile.

Materials and methods

Sixty-four patients undergoing routine double-contrast knee arthrography were included in the study. Each patient was injected, via a lateral approach, with 6 ml of Iohexol and 40 ml of air. Antero-posterior, lateral and meniscal projections were obtained.

The patients, matched for age and sex, were randomized into two groups. In the first group a needle was re-inserted into the knee joint and the air was aspirated at the end of the procedure; in the second group the air was left in the joint. All the knees were strapped in a support bandage prior to leaving the department. Each patient was given a questionnaire to complete and return in a pre-paid envelope. This documented a subjective assessment of pain during, immediately after, 48 h after and 7 days after the procedure. If present, details of site, duration and nature of the pain were requested. Comparison with any pain of the presenting complaint was also made.

A further form was completed by the radiologist indicating patient details, problems encountered and

study group. The arthrographic findings were also recorded after the radiographs were jointly viewed by the two radiologists.

Results

Of the 64 patients included in the trial, 12 were excluded because of failure to return the questionnaire. This left 52 patients, 27 in the non-aspirated group and 25 in the aspirated group (Table I). In the non-aspirated group, six (22%) experienced no pain at all. Of the rest, 41% were asymptomatic at 7 days.

In the aspirated group, 12 (48%) experienced no pain at all. Of the rest, 16% were asymptomatic at 7 days. By 7 days a total of 17 (63%) of the non-aspirated group and 16 (64%) of the aspirated group were asymptomatic.

The finding of six totally pain-free patients in the non-aspirated group as compared with 12 in the aspirated group was found to be highly significant on statistical analysis.

The arthrographic findings were similar in the two groups.

Table I. Results

	Non-aspirated	Aspirated
Total	27	25
Pain-free throughout	6 (22%)	12 (48%)
Pain-free at 48 h, but subsequently developed pain	3 (11%)	1 (4%)
Pain at 48 h, but pain-free at 7 days	11 (41%)	4 (16%)
Pain at 48 h and 7 days	7 (26%)	8 (32%)

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Discussion

Magnetic resonance imaging is now established as the gold standard for the assessment of meniscal and ligamentous injuries of the knee. However, the cost and limited availability is such that arthrography remains the imaging modality employed in many hospitals (Stoker, 1990). Assessment of pain and discomfort after double-contrast knee arthrography can only be made subjectively, and the patients were requested to exclude any pain experienced in the knee joint pre-dating the examination. In the aspirated group, 48% experienced no pain at all, compared with 22% in the non-aspirated group. It was interesting, however, that at 7 days the incidence of pain-free patients in the two groups was comparable (63% and 64%, respectively). Being pain-free at 48 h, however, was not a good sign of full recovery as all patients in this category were subsequently symptomatic at 7 days. The cause for this finding is uncertain; however, it may be due to the

patient returning to full mobility after a 48 h period of rest.

Aspiration of air must incur a minimal increased risk of infection due to a second puncture of the joint. It can, however, be done with minimal delay in finishing the examination and no additional expense.

Thus our conclusion is that air aspiration after double-contrast knee arthrography does reduce the short-term morbidity and is therefore a worthwhile exercise.

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Fascioliasis: findings in 15 patients

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Keywords: Fascioliasis, Computed tomography, Sonography

Abstract. The clinical and radiological features of 15 cases of fascioliasis are reported. Pleural effusion, associated with pulmonary infiltrates or ascites, was observed in two patients. Computed tomography (CT) was the most useful imaging method, showing small nodules and linear tracks within the liver parenchyma which were hypodense on non-enhanced scans, remaining hypodense or becoming isodense with normal liver after contrast medium administration. After successful treatment lesions decreased in number and size and finally disappeared or calcified. Lesions increased or remained unchanged when treatment failed to control the disease.

Fascioliasis is a zoonosis caused by *Fasciola hepatica*, a trematode worm that infests cattle and sheep. The disease is rare in the United States but not infrequent in Europe (Campo et al, 1984). In Spain, where the disease is relatively uncommon, most reported cases have come from the northern areas (Garcia-Rodriguez et al, 1985). Man is an accidental host in the reproductive cycle of the parasite. *Fasciola* eggs are deposited in the biliary tract of the host and passed in the stool. Under suitable conditions ciliated larvae (miracidia) develop from the ova and reach their intermediary host, the snail *Lymnaea truncatula*. Inside the snail, miracidia undergo further metamorphosis into cercariae, which leave the host and encyst as metacercariae on water plants, especially watercress. Human infection occurs usually after eating infested watercress, although other aquatic plants, horticultural species and even water may be infective. The ingested metacercariae, released from their cysts by digestive juices, penetrate the intestinal wall and migrate through the peritoneal cavity to reach the liver, perforating Glisson's capsule. The flukes then track through the liver parenchyma (invasive stage) to enter the biliary tree, where they mature and release new ova (biliary stage) usually 3 months after infestation (Aguirre, 1984; Campo et al, 1984). Ectopic migration to lung, pleura, heart, pericardium, abdominal wall, epididymis or brain may also occur (Aliaga et al, 1984).

Radiological findings in patients with fascioliasis have been reported previously (Miguel et al, 1984; Takeyama et al, 1986; Serrano et al, 1987; Van Beers et al, 1990). Nevertheless, the extrahepatic manifestations of the disease and the evolution of the hepatic lesions after therapy have not been emphasized. We report the clinical and radiographic findings in 15 cases of fascio-

liasis, including two cases with pleuropulmonary involvement. The findings and evolution of hepatic lesions on ultrasonography (US) and computed tomography (CT) are discussed.

Materials and methods

We retrospectively reviewed the clinical records and results of 15 cases of fascioliasis diagnosed at our hospital between 1982 and 1989. There were seven men and eight women, 16-64 years old. The diagnosis was based on positive indirect haemagglutination titre, (higher than 1/160) in 13 cases (range 1/640-1/20 000) and by positive double diffusion and radial immunodiffusion in two cases. Confirmation of diagnosis was obtained by a positive different serological test (immunoelectrophoresis, radial immunodiffusion or double diffusion) in nine patients and by liver biopsy in two patients. Treatment was with *Bithionol (40 mg/kg bodyweight, given on alternate days for 14 doses) (13 patients), *Praziquantel (75 mg/kg, one administration) and Bithionol (one patient) and Emetine hydrochloride (1 mg/kg by intramuscular injection for 8 days) (one patient). Good clinical response to treatment was assumed to reinforce the diagnosis of fascioliasis. Response to treatment was determined by clinical follow-up and laboratory data including blood eosinophil count, stool examination for *Fasciola* eggs (Janeckso-Urbanyi method) and serology. Hepatobiliary imaging was done in all patients before treatment, including radionuclide liver scans (six patients), liver US (14 patients) and abdominal CT (11 patients). Six patients had contrast medium enhanced CT alone; five had plain CT scans followed by contrast medium enhanced scans. Imaging studies were done 1-3

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*Editors note. It is understood that in the United Kingdom Praziquantel (Biltricide®, Bayer) is available only on a named patient and named consultant basis, and that Bithionol, a Japanese drug, is not generally available.

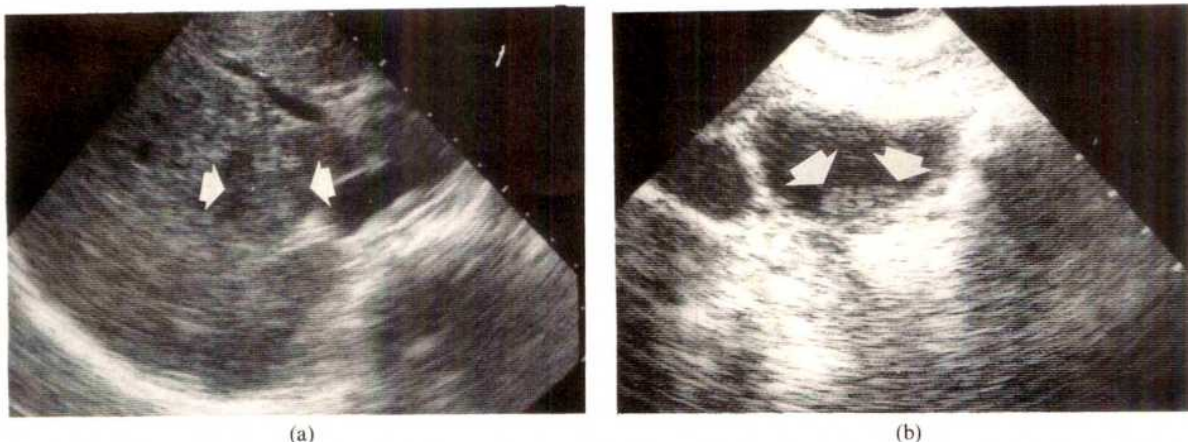


Figure 1. (a) A hypoechoic nodule (arrowheads) near the porta hepatis. (b) Presumed fluke in the gallbladder. An echogenic lesion (arrows) is shown in the gallbladder lumen. Spontaneous motility was observed on real-time examination.

months after the onset of symptoms (presumed invasive stage) in 14 patients, and at 5 months (presumed biliary stage) in one patient. Follow-up CT studies were done in eight patients.

Results

Relevant epidemiological data included residence in rural areas (13 cases) and ingestion of polluted water or horticultural products irrigated with contaminated water (10 cases). Watercress ingestion was reported in one case. Most patients presented with non-specific symptoms: dyspepsia and diffuse abdominal pain (six), asthenia and weight loss (three), right upper quadrant pain (two) and fever of unknown origin (one). Three patients were asymptomatic. Clinical signs were also non-specific; liver enlargement was found in five patients, fever in six and pleural effusion in two. Blood eosinophilia (18–70%), present in 14 of 15 patients, was the most common and significant laboratory result. In three patients, eosinophilia was the only abnormality observed. Liver enzymes were mildly elevated in 10 patients and normal in five. *Fasciola* ova were isolated from the stools in three cases.

Two patients had pleuropulmonary fascioliasis with pleural effusion. Parenchymal infiltrates in the lower lobes of the lung were also found in one case, and a small amount of ascites was detected by US in another. The pleural fluid and ascites had high levels of eosinophils. Both patients also had hepatic invasion demonstrated by CT and liver biopsy.

Radionuclide liver scans showed photopenic defects in two of six patients, and were normal in the other four. US disclosed nodular hypoechoic and peripheral parenchymal lesions in five of 14 patients (Fig. 1a). Calcifications were found in one patient. In two patients gallbladder sonograms showed oval lesions without acoustic shadowing, which had spontaneous motility and disappeared on follow-up examinations (Fig. 1b). They probably represented flukes in the gallbladder lumen, although this was not confirmed pathologically.

CT demonstrated parenchymal lesions in nine of 11 patients, and was normal in two others. Two types of lesions were found on CT: small nodules (1 cm or less), observed in all nine patients, and tortuous linear tracks present in six cases (Fig. 2). Both lesions were hypodense on non-enhanced CT, predominantly peripheral, and were more common in the right lobe of the liver. Clustered nodules produced larger hypodense areas (2–4 cm) in two cases. After intravenous contrast medium some lesions remained hypodense, being more clearly defined, whereas others became isodense with normal parenchyma. Eccentric calcification of lesions was observed in one case.

All hepatic lesions were detected during the invasive stage of the disease, except in one case who had hepatic lesions and positive stool examination for *Fasciola* ova 5 months after onset of symptoms. Conversely, gallbladder flukes and *Fasciola* eggs in the stool were observed in the invasive stage in another patient.

After treatment complete remission of the disease was achieved in 13 patients, as indicated by the absence of



Figure 2. Hypodense nodules (arrows) and linear tracks (arrowheads) are shown in non-enhanced CT of the liver.

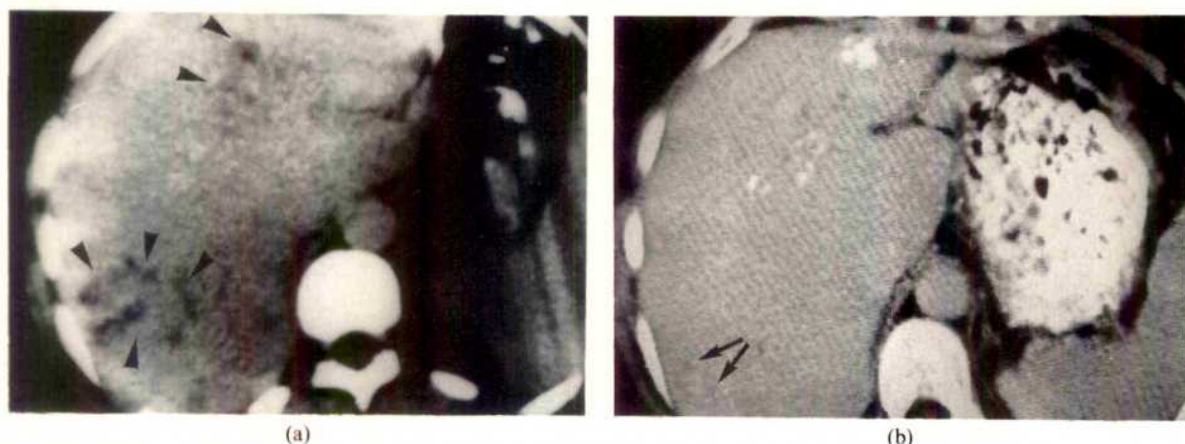


Figure 3. (a) Enhanced CT before treatment shows lesions in right and left lobes of the liver (arrowheads). (b) After treatment with Bithionol, most lesions disappear. Lesions in the left lobe became grossly calcified. Small residual hypodense nodules are seen in the right hepatic lobe (arrows).

eosinophilia, no *Fasciola* ova in the stool, low titres on indirect haemagglutination tests and good clinical conditions. CT follow-up was available in six of these patients. In four, CT showed progressive reduction in the number and size of lesions and finally their disappearance or calcification after 7–14 months (Fig. 3a,b). CT showed no change in the two patients who had a normal CT before treatment. Two other patients had recurrent disease after treatment with Praziquantel and Bithionol. In these cases CT showed an increase in the number and size of lesions in one case and persistent lesions in the other. These lesions decreased and calcified after an additional successful cycle of Bithionol with remission at 33 and 36 months, respectively, in these patients. Tiny residual hypodense nodules were observed in three patients.

Discussion

Most epidemiological and clinical findings in our series were similar to those previously reported. However, the low incidence of watercress ingestion and the presence of pleuropulmonary disease and ascites were noteworthy. Watercress ingestion is a common finding in fascioliasis (Garcia-Rodriguez et al, 1985). Nevertheless, the ingestion of uncooked horticultural species irrigated with polluted water may represent a common unrecognized way of infection, as occurred in our series. Pleuropulmonary disease is uncommon in fascioliasis with only 30 cases reported (Aliaga et al, 1984). Parenchymal infiltrates resembling the Loeffler syndrome and pleural effusion are the most common radiological features. Pneumothorax and pulmonary abscess have also been reported. Migration of *Fasciola hepatica* to the pleura and lung is considered the cause of these complications, although hypersensitivity reactions to *Fasciola* antigens may also be implicated (Campo et al, 1984; Aguirre, 1984; Aliaga et al, 1984). Confirmation of an ectopic location of *Fasciola* in pleura or lung was not obtained in our cases, but the

radiographic signs disappeared after treatment with Bithionol. Ascites is also uncommon in fascioliasis, but not surprising as the peritoneum is the usual way of migration of the parasite towards the liver.

The diagnosis of fascioliasis is based on serology (Garcia-Rodriguez et al, 1985). The indirect haemagglutination test, which has a 100% sensitivity and 97% specificity when the metabolic antigen of *Fasciola* is used, is the method of choice (Aguirre, 1984). The use of additional serological techniques may improve specificity (Garcia-Rodriguez et al, 1985).

Imaging techniques in fascioliasis are requested mainly for evaluation of hepatic invasion. The findings are different in the invasive and biliary stages (Van Beers et al, 1990). However, both stages may overlap and findings of invasive and biliary fascioliasis may coexist in the same patient, as in two of our cases. Hepatic lesions are produced by migration of the trematodes through the liver and predominate in the invasive stage. Histologically they correspond to microabscesses and tunnel-like areas of parenchymal necrosis surrounded by inflammatory infiltrates with abundant eosinophils (Serrano et al, 1987). These lesions produce photopenic defects on radionuclide liver scans, hypoechoic nodules on US and nodular or linear hypodensities on CT (Miguel et al, 1984; Takeyama et al, 1986; Serrano et al, 1987). The nodular lesions are non-specific, but linear tracks are suggestive of fascioliasis and should prompt serological confirmation. Thickening of the liver capsule and subcapsular haematoma have also been reported (Van Beers et al, 1990). In the biliary stage of the disease US seems to be more useful than CT and may show flukes in the biliary tree or gallbladder. Biliary duct dilatation and irregular wall thickening may also be demonstrated by US and CT, but these findings are non-specific (Van Beers et al, 1990).

CT is useful in the follow-up of a patient's response to treatment. After successful therapy the hepatic lesions

diminish in size and number and begin to calcify. Disappearance or complete calcification of lesions on CT correlates with correction of clinical and laboratory data indicating the eradication of the parasite. However, in some cases a few tiny lesions may remain unchanged, probably representing foci of periportal fibrosis (Serrano et al, 1987). Recurrent disease shows on CT as persistence or increase in the number or size of lesions.

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Prenatal diagnosis of nuchal cystic hygroma

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Abstract. Twenty-seven cases of nuchal cystic hygroma were diagnosed prenatally over a 5-year period at the Birmingham Maternity Hospital. Karyotypes were obtained in 20 cases, of which 14 (70%) were abnormal. Two-thirds of these represented various trisomy syndromes in contrast to other series where cases of Turner's syndrome have predominated. Twenty pregnancies were terminated. There was one intra-uterine death and two neonatal deaths. Hydrops was present in 15 cases, none of which survived to term. Associated structural abnormalities, mainly skeletal, renal and cardiac, were present in 18 cases. There were four long-term survivors with good quality of life, including both normal and abnormal karyotypes. *In utero* regression of the hygroma was documented in five cases, total in three and subtotal in two cases born with residual neck webbing.

Ultrasound is now recognized as the most effective component of antenatal screening programmes for fetal abnormality. A wide range of structural abnormalities can be identified confidently in the second trimester and with transvaginal scanning are now being detected in the first trimester. One such abnormality is fetal cystic hygroma (Campbell & Pearce, 1983; Rottem & Bronshtein, 1990). Characteristically this appears as a bilocular or multilocular cystic structure in the nuchal region with variable extension onto the thorax (Fig. 1). Rarer locations include the axilla, mediastinum, inguinal and retroperitoneal areas (Singh et al, 1971). The sonographic differential diagnosis of nuchal hygroma lies mainly between occipital encephalocele and cervical meningocele but should also include cystic teratoma, haemangioma and branchial cleft cysts (Sabbagha et al, 1980).

While the pathophysiology of fetal cystic hygroma is now understood to a certain extent, the prognostic implications of its detection remain uncertain. We present our own series of 27 cases diagnosed over a 5-year period.

Materials and methods

The Birmingham Maternity Hospital has an annual delivery rate of 5500 derived mainly from the Central Birmingham catchment area. The hospital, however, also acts as a regional referral centre for prenatal ultrasound diagnosis and 1200 detailed ultrasound assessments are performed each year. Equipment used includes real-time linear array and sector scanners with probe frequencies of 3.5 and 5.0 MHz (Acuson, Hitachi, IGE).

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Requests for detailed assessment were accepted in known high-risk pregnancies, e.g. diabetics, epileptics, multiple pregnancies and where there was a history of previous fetal abnormality. High serum alpha fetoprotein (AFP) results generated a considerable proportion of the workload but in many cases the request was for clarification of an abnormality already suspected from routine screening at a District General Hospital.

Counselling was provided both before and after the ultrasound assessment. In some cases a karyotyping procedure, either amniocentesis or placental biopsy, could be offered immediately following confirmation of a fetal anomaly but when termination was felt to be the appropriate management often no invasive karyotyping procedure was undertaken antenatally.

The outcome of pregnancy was determined from examination of the mother's notes, obtaining if possible a description of the fetus after delivery together with any post-mortem findings and the results of any further karyotyping procedures.

Results

Over a 5-year period (June 1984-June 1989) a firm ultrasound diagnosis of fetal cystic hygroma was made in 27 pregnancies (summarized in Table 1). Mean maternal age was 27 years (range 18-39 years). Mean gestational age at diagnosis was 19 weeks, the earliest diagnosis being made at 10 weeks (Fig. 2).

In 17 cases the diagnosis was confirmed by external examination after delivery. Two further cases showed gross hydrops at delivery, which may have masked the initial nuchal hygroma. In three cases no evidence of nuchal hygroma could be found, but in two of these regression had already been documented *in utero*. In the remaining five cases, all terminations, no adequate description of the fetus could be found.

Karyotyping was performed in 23 of the 27 cases but three cultures failed. Fourteen of the 20 karyotypes

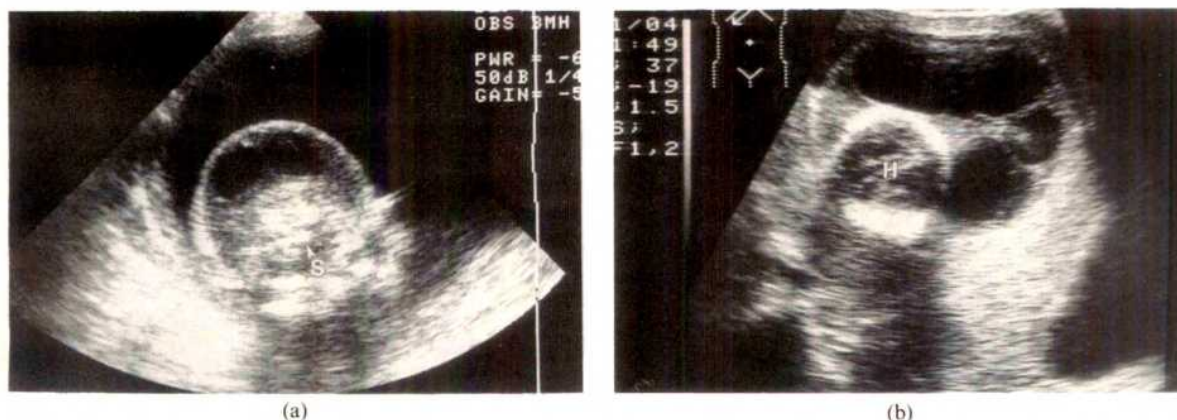


Figure 1. (a) Transverse section of fetal neck showing a bilocular cystic hygroma (S = spine). (b) Transverse section of fetal occiput showing a multilocular cystic hygroma (H = head).

(70%) were abnormal. Four of these proved to be examples of Turner's syndrome (45XO) with one further Turner mosaic (45XO/46XX). The bulk of the abnormalities (8/14), however, proved to be trisomies, with three cases of trisomy 21, three cases of trisomy 18, and

two cases of trisomy 13. The final karyotypic abnormality consisted of additional material on chromosome 5.

Twenty of the 27 pregnancies were terminated. There was one documented intra-uterine death (IUD), a case

Table I. Details of fetal cystic hygroma pregnancies studied

Case	Gestational age at diagnosis (weeks)	Karyotype (method)*	Fetal hydrops	Other anomalies	Pregnancy outcome
1. MD	19	45XO (1)	—	+	FTND
2. DS	13	45XO (3)	+	+	TOP
3. LC	19	45XO (2)	+	+	TOP
4. JS	20	45XO (3)	+	+	TOP
5. MM	12	45XO/46XX (1,2)	—	—	TOP
6. SB	17	47XX+21 (1)	+	+	TOP
7. KA	18	47XX+21 (1)	+	N/K	TOP
8. BB	20	47XY+21 (1,2)	—	+	TOP
9. LO	16	47XY+18 (3)	+	+	TOP
10. HT	18	47XX+18 (1)	+	N/K	TOP
11. MM	14	47XX+18 (1)	+	+	TOP
12. JS	17	47XX+13 (1)	+	+	IUD
13. AY	14	47XX+13 (1)	—	+	TOP
14. CF	16	46XX5q+ (1)	+	+	TOP
15. JH	21	46XY (1,3)	—	N/K	TOP
16. ES	19	46XY (3)	+	N/K	TOP
17. HV	17	46XY (1)	—	+	FTND
18. JL	16	46XY (1)	—	—	FTND
19. JR	17	46XY (1,2)	+	+	TOP
20. LF	10	46XY (2)	—	—	TOP
21. TB	38	—	+	+	NND
22. FB	34	—	+	+	NND
23. RD	21	—	—	—	FTND
24. MD	18	No growth (3)	—	+	TOP
25. RS	20	No growth (3)	+	+	TOP
26. ZB	23	No growth (3)	—	+	TOP
27. SR	17	—	—	N/K	TOP

* (1) = amniocentesis; (2) = placental biopsy; (3) = post-mortem tissue biopsy.

TOP = termination of pregnancy; IUD = intrauterine death; NND = neonatal death; FTND = full-term normal delivery; N/K = not known.

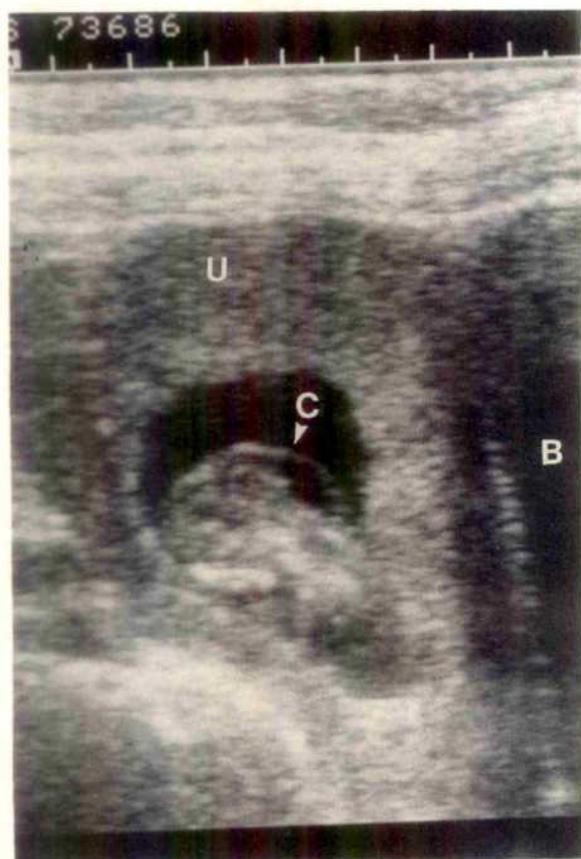


Figure 2. A 10-week embryo in longitudinal section showing a distinct cystic structure extending from the occipital region onto the thorax (C = cystic hygroma, U = uterus, B = bladder).

of trisomy 13 in a twin pregnancy, but IUD was thought to have occurred in several of the terminated pregnancies judging by the degree of fetal maceration present at delivery. Two deaths occurred in the early neonatal period, both infants being born with hydrops.

Generalized hydrops was present either at diagnosis or by delivery in 15 cases, none of which survived. In 18 of the 20 cases where adequate descriptions were available, additional structural abnormalities, mainly skeletal, cardiac and renal, were noted (Table II).

There were four long-term survivors. Residual neck webbing was seen in two cases, one a Turner's syndrome with known renal anomalies (multicystic dysplastic kidney and mild pelvi-ureteric junction obstruction), which continued to term, the other case having a normal male karyotype. This infant, however, has since been diagnosed as a case of Noonan's syndrome with mild pulmonary stenosis and a small atrial septal defect. The other two survivors were both male although a normal karyotype was confirmed in only one of them. In both cases the initial small hygroma was seen to regress *in utero* and external examination at delivery was entirely

normal. The subsequent development of both these infants has been unremarkable.

Discussion

Fetal cystic hygromas are thought to develop as a consequence of a "jugular lymphatic obstruction sequence", (Bill & Sumner, 1975). By Day 40 of normal embryological development, communication is established between the jugular lymphatic sacs and the internal jugular veins. If this communication fails to develop, the lymphatic sacs distend with the formation of visible hygromas and subsequent development of generalized lymphoedema with pleural effusions and ascites (Fig. 3). By this stage fetal demise is imminent and our series confirms the findings of previous studies (Chervenak et al, 1983; Garden et al, 1986; Abramowicz et al, 1989; Cohen et al, 1989) with no survivors seen in the group with hydrops.

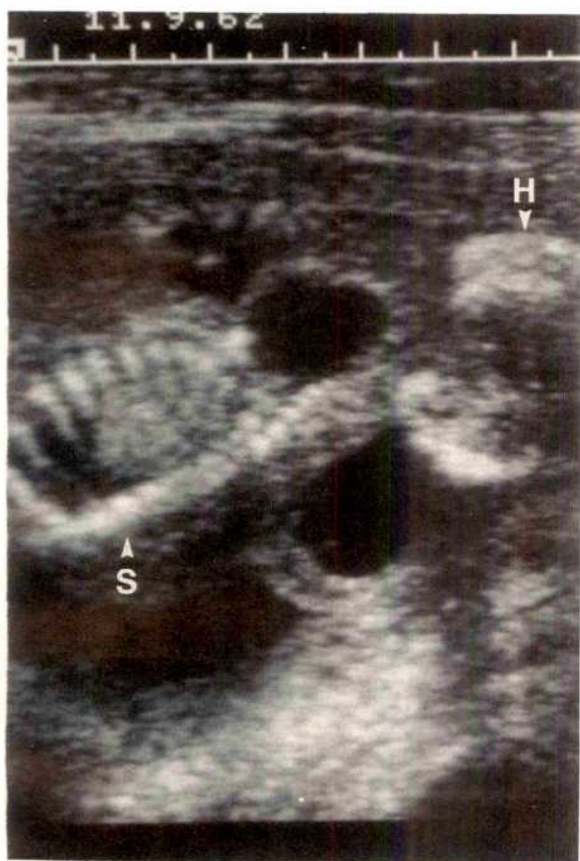
A fetal nuchal hygroma thus indicates a generalized disorder of lymphatic development and is a different entity from the hygromas encountered in paediatric practice, which represent localized lymphangiomatous malformations and are usually amenable to surgical resection (Emery et al, 1984).

Not surprisingly a variety of factors have been found to influence the development of the lymphatic system. Fetal cystic hygroma has been described as a feature of a number of rare single gene disorders including the lymphoedema distichiasis syndrome, Robert's syndrome and the multiple pterygium syndrome. Certain teratogens have been implicated including alcohol, trimethadione and aminopterin. The best known association is with the Ullrich Turner syndrome (45XO) but hygromas have also been documented in other chromosomal disorders including trisomies 21, 18, 13 and 22, as well

Table II. Associated structural abnormalities

Abnormality	No. of cases	Survivors	Description
Renal	6*	1	Midline kidney (2), hydronephrosis (3), hydroureter (1), multicystic kidney (1)
Skeletal	6*	0	Flexion deformities (4), talipes (1), rocker bottom feet (1), syndactyly (1), micrognathia (2)
Craniofacial	8	0	Microcephaly (4), cleft lip/palate (3), hypertelorism (1)
Cardiac	3	1	Fallot's tetralogy (1), hypoplastic left heart syndrome (1), pulmonary stenosis/ASD (1)
Body wall	2	0	Exomphalos (2)

*Includes cases with multiple abnormalities.



(a)



(b)



(c)

Figure 3. The jugular lymphatic obstruction sequence. (a) Coronal section of 18-week fetus showing large bilateral nuchal hygromas (H = head, S = spine). (b) Same fetus in longitudinal section showing pleural effusions and ascites (S = spine, E = effusion, A = ascites, L = liver, G = gut). (c) Transverse section of fetal abdomen showing lymphoedema (skin thickness 17.3 mm) with ascites outlining the echogenic gut (A = ascites, G = gut).

as in a range of partial deletion syndromes (Chervenak et al, 1983).

The figure of 70% abnormal karyotypes in our series agrees closely with the findings of previous studies. In two recent reviews of the world literature (Abramowicz et al, 1989; Cohen et al, 1989) cases of Turner's syndrome have predominated, constituting up to 75% of the abnormal karyotypes. In our series, however, various trisomy syndromes predominated, constituting two-thirds of the abnormal karyotypes.

This discrepancy may simply reflect the improved resolution of modern ultrasound equipment as several of the hygromas in our series were small (10–15 mm) at diagnosis (Fig. 4), but it is, in our opinion, a true reflection of the incidence of trisomies in the study population. With the advent of first-trimester trans-

vaginal scanning, we anticipate further reports linking nuchal hygroma with the trisomy syndromes, particularly in the light of one recent report (Rottem & Bronshtein, 1990) where routine transvaginal scanning of 1652 fetuses between 9 and 16 weeks gestation yielded 20 examples of cystic hygroma, which was thus the commonest congenital malformation detected (30%).



Figure 4. Transverse section of 17-week fetus showing small (12 mm) bilateral cervical hygromas (S = spine, C = cystic hygroma).

Karyotypic results were, unfortunately, not presented in this study but the incidence of trisomies as well as other chromosomal anomalies is known to be proportionally higher in the first trimester than in the second. Fetal loss in the first trimester is higher in karyotypically abnormal fetuses.

Over the years there have been isolated reports of *in utero* regression of a documented cystic hygroma (Chervenak et al, 1983; Rodis et al, 1988). Such regression may occur with belated development of the normal venous communication. The presence of other structural anomalies, however, has often resulted in fetal demise or poor quality of postnatal life and in only a handful of cases has a favourable clinical outcome been documented (Chodirker et al, 1988; Distell et al, 1989; Macken et al, 1989). These cases include, however, both normal and abnormal karyotypes. Our series now adds five further examples of documented *in utero* regression,

four of which were associated with a favourable clinical outcome despite the presence of renal anomalies in one case and minor cardiac anomalies in another. Cases included both normal and abnormal karyotypes, namely a Turner's syndrome and a Turner mosaic fetus, in which pregnancy was terminated.

Conclusion

The antenatal detection of nuchal cystic hygroma continues to carry a poor prognosis, particularly if associated with hydrops when fetal demise is often imminent. If the hygroma is small at diagnosis and if there is some evidence of regression *in utero*, however, a favourable clinical outcome may be seen in a few selected cases. The presence of an apparently isolated small hygroma should prompt a detailed search for other subtle structural anomalies which may point to one of the trisomy syndromes—in particular, renal and cardiac abnormalities. The high proportion of abnormal karyotypes (70%) in our series emphasizes the need for some form of karyotyping procedure to be carried out in all cases. Similarly, the range of associated structural abnormalities indicates the need for accurate post-mortem information in all cases of fetal demise, including terminations. Only when full karyotype and post-mortem information is available can we hope to identify the underlying syndrome and provide accurate counselling concerning the probable outcome of future pregnancies.

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Dosimetric accuracy at low monitor unit settings

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Abstract. Dosimetric accuracies at low monitor units are evaluated for linear accelerators from various manufacturers. A large error is observed in the majority of the accelerators. The error can be positive or negative. Although the error can exceed 20% for the first few monitor units, it is usually less than 5% when more than 10 monitor units are delivered. When low doses are required proper precautions should be taken for dosimetric accuracy including the beam energy, beam flatness and dose per monitor unit.

To optimize tumour-cure probability an uncertainty of $\pm 5\%$ in tumour dose and $\pm 2\%$ in radiation dosimetry is often recommended in clinical situations (Task Group 21, 1983; WHO, 1988). Achieving this level of accuracy depends on the understanding of various uncertainties in the dosimetric parameters. Most of them have been discussed in the literature. One consideration that is usually ignored, even in the recent publications (IPSM, 1988; WHO, 1988), is the accuracy of dose delivery at low monitor unit (MU) settings from medical linear accelerators. For MU settings < 50 , the actual delivered dose could vary significantly for some linear accelerators and may fall beyond the limit of acceptable accuracy. Ideally, dose delivered per unit MU should be constant. Since MU are integer numbers and can be set only to the nearest unit, the uncertainty increases as fewer MU are set. However, for most accelerators there seems to be an additional definite non-linearity.

Situations do arise where < 50 MU are delivered during dosimetric applications, research and patient treatment. While using fast film for radiation protection dosimetry low MU are typically used. For thermoluminescent dosimeter (TLD) dosimetry, often low doses (MU) are used for calibration. In patient treatments using multiple fields, the MU/field may be < 50 . Ohara et al (1989) used time gated low exposure of 3, 5, and 10 MU to avoid geometric miss in thoracic tumours resulting from diaphragm movement caused by respiration. In other clinical situations like chronic myelocytic leukaemia (CML) and polycythemia vera the dose per fraction is as low as 25 cGy. This means the MU per field is in the range of 8-15 MU depending upon patient thickness and technique used. Johnson (1977) showed that in CML small doses can cause appreciable cytopenias leading to patient death. Hence, to avoid any serious complications the dose delivery must be accurate. Finally when an accelerator is not functioning properly, multiple restarts may be attempted to complete the prescribed dose. In such situations only a few MU are delivered at a time.

Whenever low monitor units are used it is important to know the uncertainty in the actual dose. This project was undertaken to evaluate the dosimetric accuracy at low MU settings for several medical linear accelerators.

Methods

To study the dosimetric linearity (dose/MU) at low MU of a linear accelerator, measurements were performed as described in Task Group 21 (1983). Dose in a medium at a point is given as:

$$D_{\text{med}} = Q N_{\text{gas}} (\bar{L}/\rho)_{\text{gas}}^{\text{med}} P_{\text{ion}} P_{\text{rep}} P_{\text{wall}} \quad (1)$$

where Q is the average measured charge corrected for temperature and pressure, N_{gas} is the cavity gas calibration factor, $(\bar{L}/\rho)$ is the restricted stopping power ratio of medium to chamber gas, P_{ion} is a correction for ion recombination, P_{rep} is the replacement correction factor, and P_{wall} is a correction for the chamber wall. All of these parameters are discussed in Task Group 21 (1983). If we assume all the parameters are constant for a specific machine and energy, then D_{med}/Q should be constant. The validity of this assumption is explained in the discussion section. For a few selected units, beam energy, P_{ion} , and $(\bar{L}/\rho)$ were evaluated at various MU settings.

Any deviation from a constant value of the measured dose/MU of a machine could be due to: (i) the ion chamber; (ii) the electrometer and (iii) the machine. Dosimeter linearity is essential and has been discussed in the literature (Massey, 1970; Orton & Seibert, 1972; IPSM, 1988; WHO, 1988). It is expected that for a beam energy the dosimeter linearity should be within $\pm 1\%$ over the working range. For a small volume ion chamber operating at high collecting voltage (> 300 V) the limit is easily achievable. In this study it was assumed that the 0.6 cm³ Farmer-type ion chambers are very linear with dose rate and charge collection (see discussion section). For the high precision electrometers, corrections were made for non-linearity in the different

range settings. It was accounted for by accumulating charges with different range settings for the same MU.

All measurements were performed in a standard calibration set-up at the respective reference points as outlined in Task Group 21 (1983). Measurements were taken from the lowest allowed MU setting up to 400 MU at the clinically used dose rates (200–300 MU/min) for a variety of accelerators from several manufacturers. In most cases a 0.6 cm³ PTW cylindrical ion chamber (Nuclear Associates, Carle Place, NY) was used as the dosimeter and Keithley (Keithley Instrument Co., Cleveland, OH) high precision electrometers were used for the measurement of the charge. For the lower MU settings, high sensitivity scales were used. Several sets of readings were taken for each data point to achieve suitable statistics. The per-

centage uncertainty in any data set was $< \pm 0.5\%$ and it was not plotted in figures. From the above assumption, Q/MU was taken as a measure of dose per MU. Different accelerators with the same stated beam energy were included in this study. The beam energies studied were 4, 6, 10 and 18 MV.

Results

The dose non-linearity cannot be visualized if the normalized charge (normalized to 1.0 at 100 MU) is plotted vs. MU on a log-log scale. However, if the same data are plotted differently the non-linearity becomes obvious. Parts (a), (b), (c) and (d) of Fig. 1 are semilog plots of dose/MU vs. MU for 4, 6, 10 and 18 MV beams, respectively. There seems to be no correlation between the photon energies and the behaviour of the

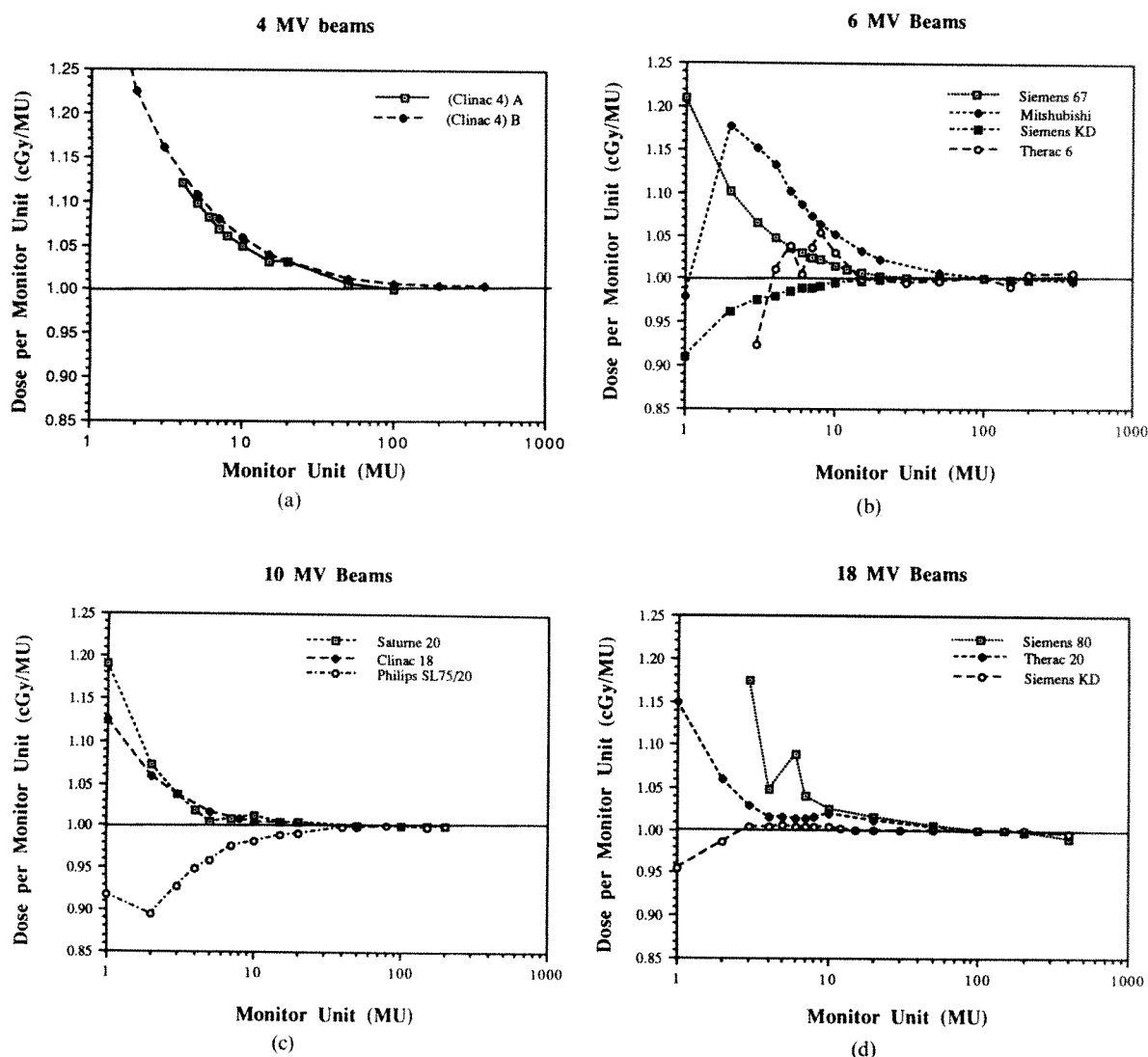


Figure 1. Plot of dose/MU vs. machine MU for (a) 4 MV, (b) 6 MV, (c) 10 MV and (d) 18 MV photon beams.

dose/MU curve. The results are machine specific. In most cases the error is greatest at lowest MU.

Discussion

The large deviation in dose/MU from 1.0 at low MU could be due to machine non-linearity. This deviation is the dosimetric error caused by the integer nature of MU and the machine performance at low MU. This error can be called monitor unit error, δ , similar to that of the timer error for tele-isotope machines (Massey, 1970; Orton & Seibert, 1972). If the error, δ , is constant, it can be determined cautiously by any of the following methods which have been described in the literature: (1) graphical method; (2) two exposure method and (3) multiple exposure method.

If dose/MU is a smooth function, one can use the graphical method. If one uses the two exposure method, then δ can be given by

$$\delta = \frac{Q_2 M_1 - Q_1 M_2}{Q_1 - Q_2} \quad (2)$$

where Q_1 is the charge collected for M_1 MU and Q_2 is the charge collected for M_2 MU. It was shown that a better method (Orton & Seibert, 1972) is to take several multiple exposures for the same MU. If n is the number of fractions for the same MU then

$$\delta = M \left[\frac{Q_{n(M/n)} - Q_M}{nQ_M - Q_{n(M/n)}} \right] \quad (3)$$

where $Q_{n(M/n)}$ is the charge collected for n exposures of M/n MU and Q_M is the charge collected for one exposure of M MU. The calculated δ for various machines range from -0.3 to 0.7 MU in this study.

Dose in a medium, when measured with an ionization chamber, is dependent on the parameters Q , $(\bar{L}/\rho)$, and P_{ion} as described in Eqn (1). The other parameters N_{gas} , P_{rep} and P_{wall} are constant for an ion chamber. The restricted stopping power ratio, $(\bar{L}/\rho)$, is dependent on the beam energy. It has been previously observed by Barish et al (1987) that the beam energy of a given machine during the very first few MU might be different from that during steady state operation. This could be caused by a time lag in the feedback circuit and other controlling parameters.

At first glance it seems that energy change might be the main cause of dosimetric error, which should be evaluated at a fixed dose rate. For a different dose rate a machine might deliver a different dose, as reported by Cheng and Kubo (1988). Figure 2 shows the effect of photon beam energy on dosimetric parameter $(\bar{L}/\rho)$. It is a plot of restricted stopping power ratio of water to air against nominal accelerating potential. This curve is relatively flat on a linear scale. Even though $(\bar{L}/\rho)$ is a strong function of electron energy its variation for small changes in megavoltage photon energy is very minimal. The possible changes in photon energy were evaluated by measuring the ionization ratio (IR) defined in Task Group 21 (1983). The IR is identical with the beam

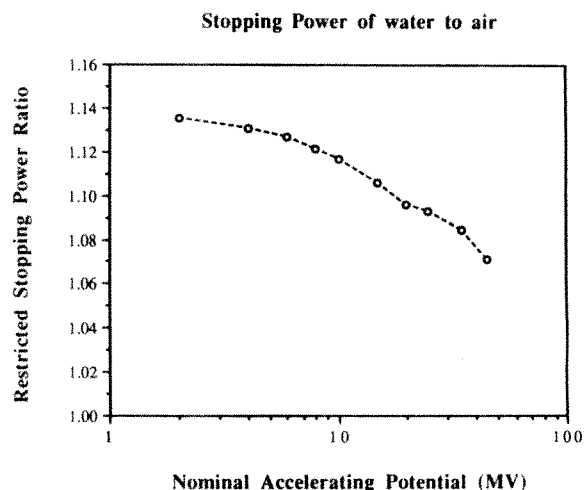


Figure 2. Restricted stopping power ratio of water to air plotted against nominal accelerating potential of various photon beams.

quality index, $I = J20/J10$ (WHO, 1988) and reciprocal to the ratio $J100/200$ (IPSM, 1988). The IR was measured at various MU settings for different machines at a fixed dose rate. Units with different bending magnet design (0° , 90° and 270° bending magnet for Clinac 4, Philips SL75/20 and Saturne-20, respectively) were included in this experiment. Based on our measurements there was no correlation between bending magnet design, type of accelerator, energy shift and MU setting. For example, a Saturne-20 unit with a dual photon beam showed an energy shift in opposite directions for its two beams. The measured shift in IR for 1 MU compared with 200 MU was -5.0% and $+1.5\%$ for 10 MV and 18 MV, respectively. Other machines showed an IR shift of 1–2% at very low MU. Obviously these changes in beam quality have very little impact on the $(\bar{L}/\rho)$ ratio (Fig. 2).

The other factor, P_{ion} , representing the ion recombination in an ionization chamber was evaluated for the majority of machines at the lowest MU settings and the MU of calibration (100–200 MU). For most cases studied, P_{ion} was within $\pm 1\%$. Based on this observation, one could conclude that P_{ion} is not sensitive for practical ion chambers operating at suitable voltage. For most accelerators the dose rate is constant and one would expect the P_{ion} to be constant. Even in a machine like Saturne-20 with variable dose per pulse this was not a major problem. This indirectly confirms the ion chamber linearity.

For the clinical situations in which time gating of the exposure is to be used (Ohara et al, 1989), the specific machine characteristics should be evaluated before this is attempted. Clinical evaluation of the dosimetric effect of low MU settings should include P_{ion} , beam energy and beam flatness as discussed by Barish et al (1987).

Machine specifications should also include the linearity of dose at lower MU setting. IPSM (1988) and

WHO (1988) recommended that units should be linear within $\pm 2\%$ from 0.1 Gy to 10 Gy. However, most non-linearity is seen below this limit (Fig. 1). Low MU linearity might be purely academic but in many situations this could cause significant error. Users are advised to check their machines for possible anomalies in beam parameters including penumbral enlargement (Tuohy & Morgan, 1990), beam energy and the dosimetry at low MU. Some accelerators have built-in interlocks which limit the minimum MU settings till a diagnostic and beam energy is verified. An additional circuit could be provided to prevent operation at lower MU when beam characteristics cannot be met. An attempt was made to include all machines from major manufacturers in this study; however, it may not be complete.

Conclusions

The variation in dose per MU is machine specific and cannot be predicted in general. Some accelerators show a pattern of constant monitor unit error, δ , typically of the order of ± 0.1 – 0.2 MU, except the Varian Clinac 4 where the error is > 0.4 MU. For some units δ is not constant, hence usual methods for determining δ cannot be used and the prediction of error is inaccurate. Machines having a large δ value require that a greater number of MU be set to achieve an acceptable limit of accuracy. While the individual beam dose may be in error, in terms of total target dose, the error may be insignificant. Only where the total treatment is made up of small MU exposures, the error in total target dose is of the same order. Therefore, in clinical situations the error introduced by dose non-linearity is of minimal concern as most treatments are > 10 MU. Where δ is large, a correction factor may be appropriate for accurate dosimetry. If a machine is not functioning properly and terminates, multiple attempts to complete the treatment should be avoided or determined with direct consultation with a physicist. Caution should be exercised when using small MU settings especially for TLD and film dosimetry. Determination of δ should also be included in the machine acceptance testing and usual quality control. It is not clear that acceptance criteria

can be established for the stability of dose/MU. However, the magnitude and constancy of the error should be determined so that approximate corrections can be made when needed. If lower doses are desired other methods such as extended distance and beam attenuation should be used.

Acknowledgment

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Tumour size as a prognostic factor in carcinoma of the cervix: assessment by transrectal ultrasound

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Abstract. Transrectal ultrasound (TRUS) was used to measure tumour size in patients with carcinoma of the cervix and to assess its prognostic significance. Clinical staging was conducted and at the time of examination under anaesthesia, TRUS was used to assess maximum transverse diameter of the tumour. Eighty-one patients were studied. FIGO stages were IB 34 patients, IIA seven patients, IIB 31 patients, IIIA two patients and IIIB seven patients. Mean tumour diameters by stage were IB 37 mm, IIA 37 mm, IIB 49 mm, IIIA 42 mm and IIIB 50 mm. There was a significant correlation between size and stage ($p=0.001$). With a median follow-up of 18 months, 16 relapses have occurred. The actuarial relapse rates at median follow-up by stage were IB 10%, IIA 17%, IIB 22%, IIIA 0% and IIIB 35%. The actuarial relapse rates by size grouping at median follow-up were less than 30 mm 0%, greater than 30 and less than 40 mm 11%, greater than 40 and less than 50 mm 22%, and greater than 50 mm 38%. There was a significant difference between the mean recorded size of the tumours in the relapsed group and the relapse-free group ($p=0.02$). Despite the small number of patients and short follow-up, tumour size as measured by TRUS appears to predict relapse.

Although tumour volume is frequently discussed as a prognostic factor in carcinoma of the cervix, very few reports have related tumour measurement to the outcome of treatment either following surgery (Piver & Chung, 1975) or radiotherapy (Homesley et al, 1980). Given this lack of data relating tumour size and prognosis, and the difficulties of making direct tumour measurements, most centres continue to report results using FIGO classification (Pettersen, 1986). Transrectal ultrasound (TRUS) has been used extensively in the assessment of carcinoma of the prostate (Griffiths et al, 1987) and recent reports have cited its usefulness in staging carcinoma of the cervix (Yuhara et al, 1987). We have used TRUS to measure the primary tumour in a group of patients with carcinoma of the cervix before radical radiotherapy. The result of treatment has been related to the measured tumour size.

Materials and methods

Eighty-one patients with carcinoma of the cervix were assessed using TRUS. All patients were conventionally staged and at the time of examination under anaesthesia. Transrectal ultrasound was conducted by an independent assessor and the findings did not influence clinical management. Transrectal ultrasound was conducted with the patient in the lithotomy position. A Foley catheter was inserted in the bladder which was then filled with 300 ml sterile water. A 4 MHz rotating transducer (focal length 3-7 cm) (Bruel and Kjaer type

1850) inserted through a rectal tube was used. A balloon around the transducer head was inflated with 50 ml water to allow optimal ultrasound contact with the anterior rectal wall. Transaxial images in a plane perpendicular to the probe were obtained. From these images the maximum tumour transverse diameter was recorded (Fig. 1). This measurement was chosen as we believe it gives the best indication of tumour size (*vide infra*) and in addition previous studies have suggested that it reliably demonstrates parametrial spread (Yuhara et al, 1987). All patients were treated with radical radiotherapy using methods previously described (Easson & Pointon, 1985). Follow-up was clinically dictated. Details of recurrence have been obtained from the patients' records.

Statistical methods

A Spearman Rank correlation coefficient was used to look for any association between stage and tumour size. The log rank test (Peto et al, 1977) was used for the survival and relapse-free times. An unpaired *t*-test was used to compare the difference in tumour size between recurrent disease and recurrence-free groups.

Results

Eighty-one patients were studied between 1986 and 1988. The age range was 22-74 years (median 51 years). Median follow-up was 18 months. Histology was available in all cases: squamous carcinoma 72 (89%), adenocarcinoma seven (9%), adenosquamous one (1%), undifferentiated carcinoma one (1%). The clinical stages are detailed in Table 1. The mean tumour diameter was

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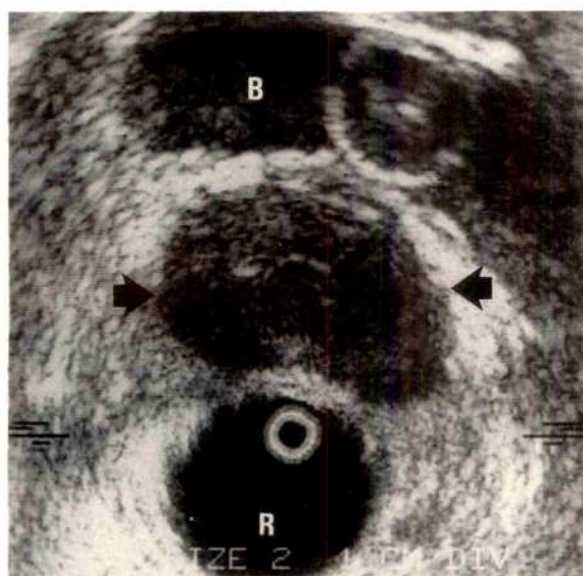


Figure 1. Transrectal ultrasound of patient with bulky stage IB carcinoma of the cervix. Arrows demonstrate the maximum transverse diameter. R is the rectum, and B is the bladder.

43 mm (range 25–75 mm). The mean tumour transverse diameters by stage are detailed in Table II. The distributions of tumours by size and stage are shown in Fig. 2. There was a significant correlation between size and stage ($p = 0.0001$).

To date there have been 16 relapses. The sites of relapse are detailed in Table III. The actuarial relapse rates at median follow-up by stage were IB 10%, IIA 17%, IIB 22%, IIIA 0% and IIIB 22%. The actuarial relapse rates at median follow-up by size were less than 30 mm 0%, greater than 30 and less than 40 mm 11%, greater than 40 and less than 50 mm 22% and greater than 50 mm 38%. Relapse-free survival by stage and size grouping is shown in Figs 3 and 4. There was no significant relationship between stage and relapse-free survival ($p > 0.4$, log rank). Size and relapse-free survival had a greater association although this did not achieve true statistical significance (overall $\chi^2 = 6.39$ (3 df), $p = 0.09$, χ^2 for a trend of 4.48 (3 df), $p = 0.03$). The mean diameter of the recurrent disease group was 49.1 mm and of the recurrence-free group 41.6 mm.

Table I. Distribution of patients by stage

Stage	Number	Percentage
IB	34	42
IIA	7	9
IIB	31	38
IIIA	2	2
IIIB	7	9

Table II. Distribution of mean tumour diameter by stage

Stage	Mean tumour diameter (mm)
IB	37
IIA	37
IIB	49
IIIA	42
IIIB	50

These groups are significantly different ($t = 2.34$, $p = 0.02$).

Discussion

Tumour size is clearly a prognostic factor in carcinoma of the cervix, both in terms of controlling the primary tumour and in predicting the likelihood of pelvic nodal involvement (Piver & Chung, 1975). Transrectal ultrasound is a convenient method of measuring tumour size and local spread. It has been evaluated

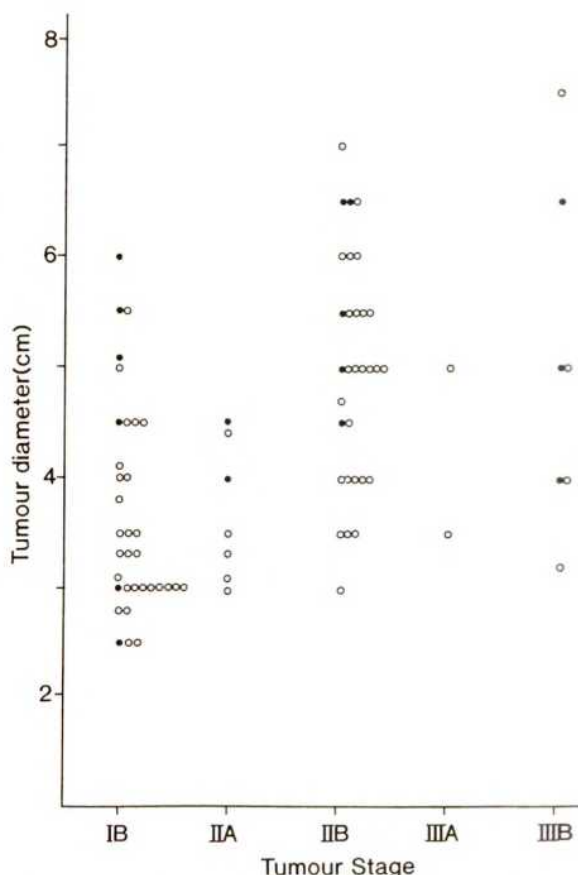
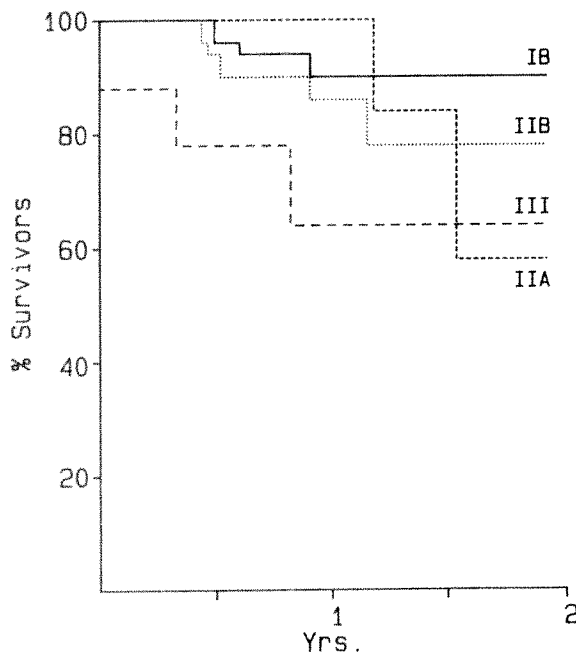
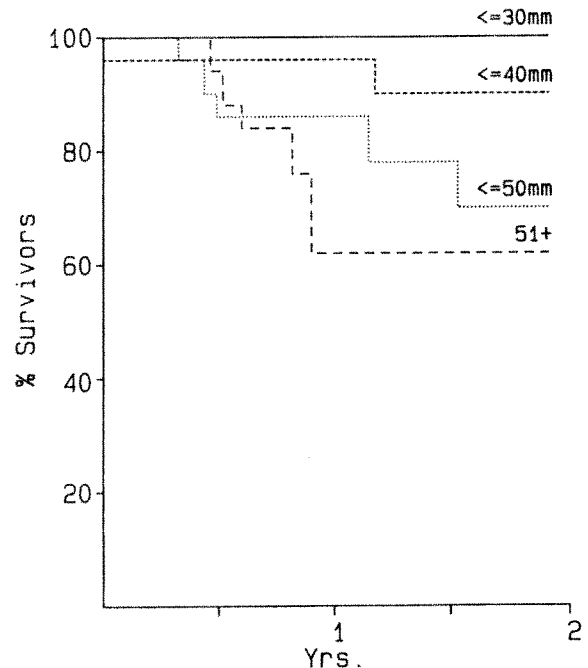


Figure 2. Distribution of tumour diameter by stage. The filled circles signify cases where relapse occurred.

Table III. Site of tumour relapse

Site	Number
Central pelvis	2
Lateral pelvis	7
Central pelvis and para-aortic nodes	1
Para-aortic nodes and metastases	2
Metastases	4

previously in carcinoma of the cervix comparing TRUS with clinical staging (Cionini et al, 1987), surgical findings (Zaritsky et al, 1979; Yuhara et al, 1987) and other imaging methods, e.g. computed tomography (CT) (Meanwell et al, 1987) and magnetic resonance imaging (MRI) (Hall-Craggs et al, 1987). It does however have certain limitations: (1) discrimination of small volume tumours from normal uterine tissue is difficult and therefore these tumours will have their size overestimated; (2) proximal extension of cervical tumours into the body of the uterus is not reliably demonstrated so cephalocaudal measurement of tumour size is uncertain; (3) anteroposterior measurement of tumour size is sensitive to angulation of the long axis of the probe which creates variation in resulting measurements. For these reasons the most reliable tumour measurement is of the maximum transverse diameter (Fig. 1). While TRUS allows assessment of parametrial extension, it is however of no value in imaging pelvic lymph node involvement, unlike CT and MRI.

**Figure 3.** Relapse-free survival by stage.**Figure 4.** Relapse-free survival by tumour diameter.

Despite the small numbers and relatively short follow-up in this study, tumour size as assessed by TRUS measurement of maximum transverse diameter appears to be a better predictor of relapse than FIGO stage and is of prognostic significance. This concurs with other studies where tumour size has been measured on surgical specimens following Wertheim's hysterectomy (Piver & Chung, 1975) or on direct clinical assessment (Homesley et al, 1980) of cervical carcinoma. This study also demonstrates the wide variation of tumour size within each FIGO stage (Fig. 2), which has implications for the comparison of results from different centres where variation in treatment results may be partially due to differing mean tumour sizes. Tumour size measurement may, in addition to stage, allow the selection of patients for new approaches to treatment, e.g. neoadjuvant chemotherapy. A study comparing clinical staging, TRUS and MRI is proceeding at this centre (Hawnaur et al, 1990).

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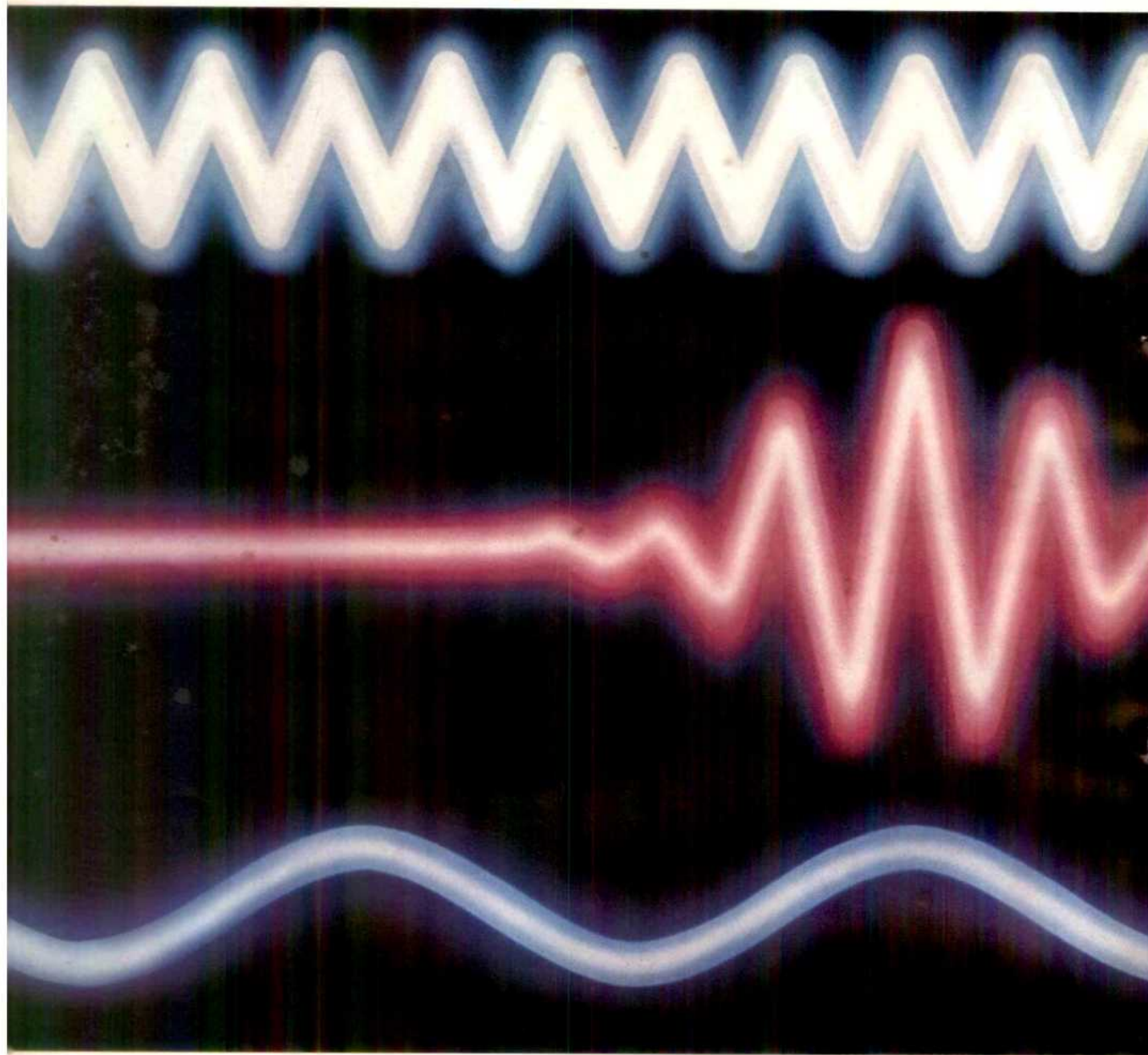
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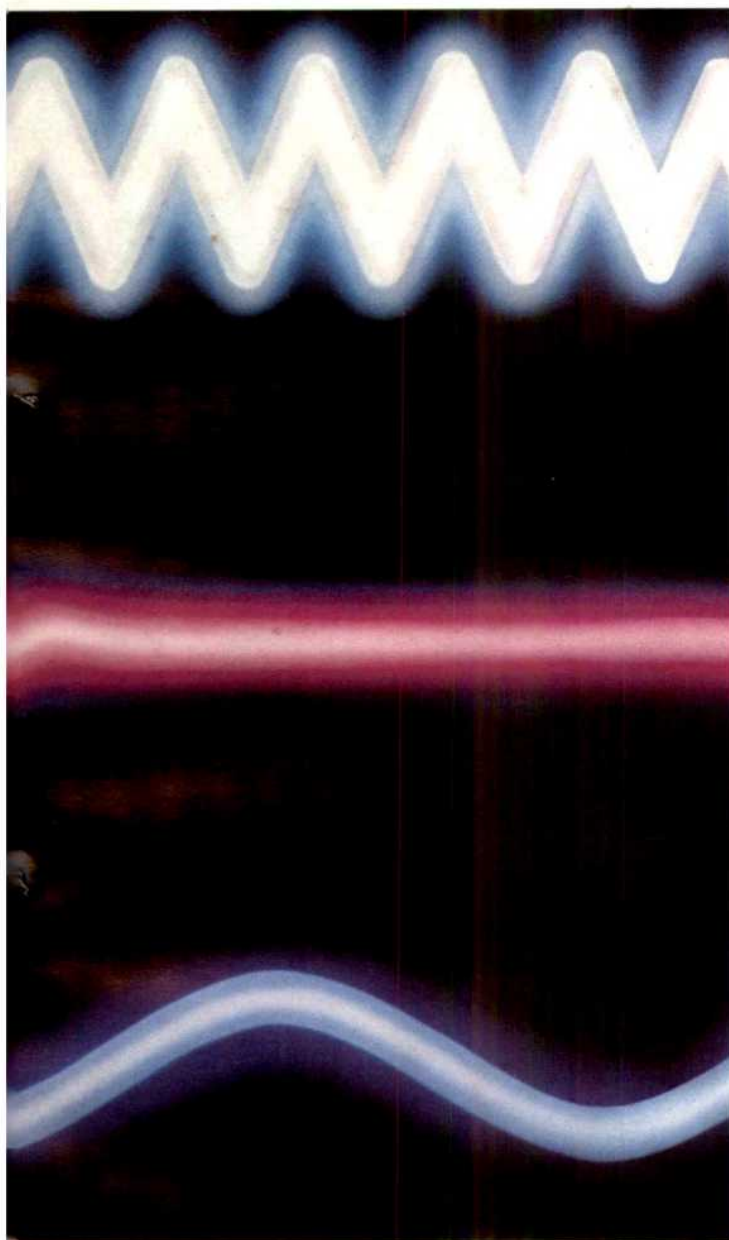
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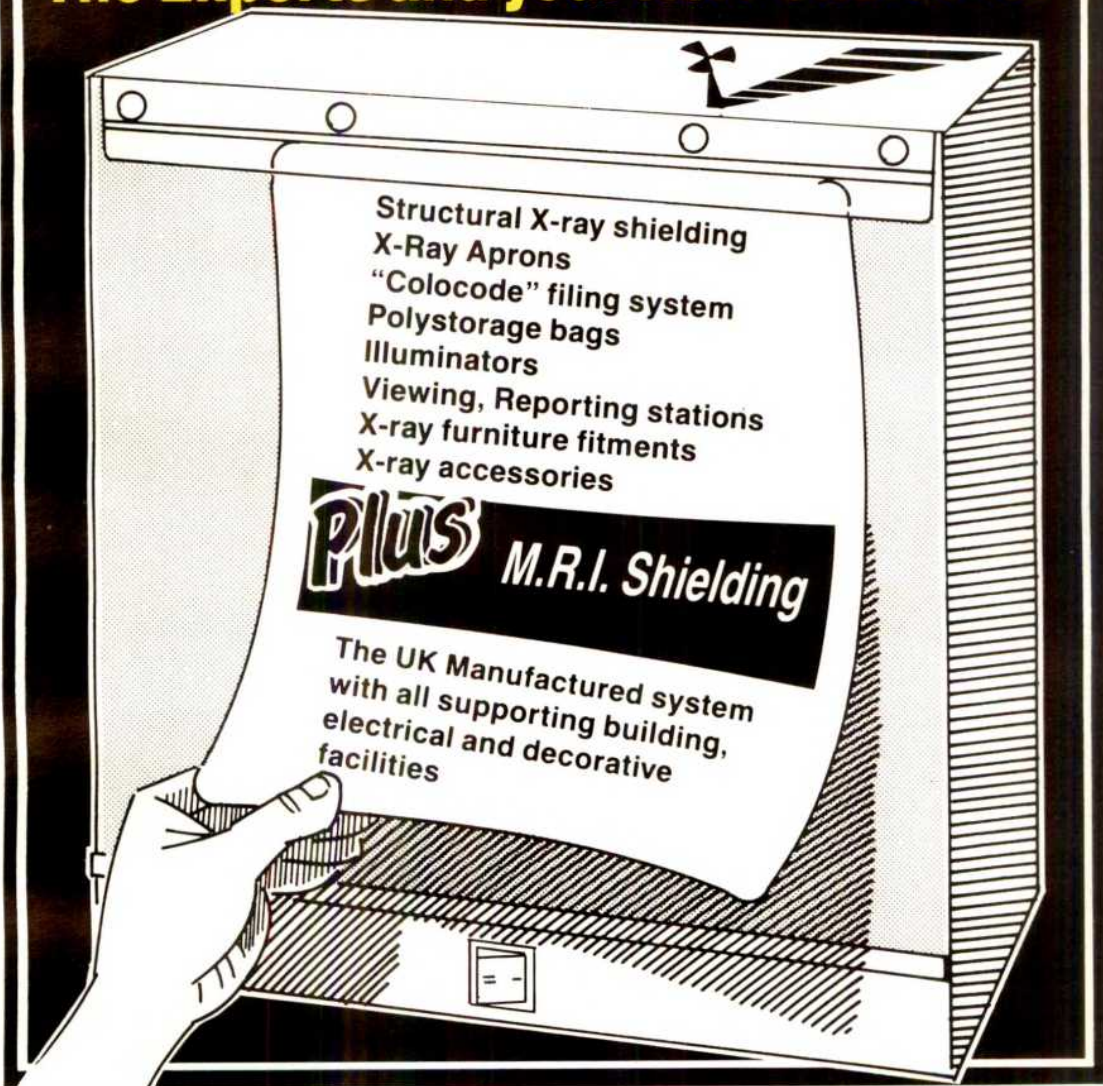
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Strontium-89 chloride for pain palliation in prostatic skeletal malignancy

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Abstract. In a multi-centre study strontium-89 was shown to be effective in relieving bone pain from prostatic carcinoma in patients who had failed conventional therapies. Of 83 patients assessed at 3 months, following the administration of a dose of at least 1.5 MBq/kg, 75% derived benefit and 22% became pain free. Symptomatic improvement usually occurred within 6 weeks and continued for between 4 and 15 months (mean 6 months). Based on the dose estimation part of this study the recommended dose of strontium-89 is 150 MBq. Toxicity was low, provided platelet levels were above $100 \times 10^9 l^{-1}$ at the time of treatment. Repeat treatments with strontium-89 may be given at intervals of not less than 3 months. Strontium-89 is administered intravenously on an out-patient basis with no special radiological protection precautions.

Carcinoma of the prostate is the commonest malignancy of the male genito-urinary tract with a probability of 1 in 40 that a man in England and Wales will develop the disease in his lifetime (Wilson, 1987). It has a high overall mortality which is increasing and is now the third most common cause of death in males in England and Wales (Office of Population Census and Surveys, 1990), and the second most common cause of death from cancer in males in the USA (American Cancer Society, 1991). It has a high metastatic potential (Jacobs, 1983), one third to one half of patients presenting with skeletal metastases. Approximately 25% of patients are initially resistant to treatment by hormones and the remainder eventually develop hormone resistance, 50% of patients surviving 3 years and less than 10% surviving 10 years (Scott et al, 1980). Of the patients who relapse whilst on hormone therapy approximately 75% develop skeletal lesions (Debruyne et al, 1988). The number of patients responding to cytotoxic chemotherapy is low and consequently few feel it has any place in routine management of bone pain (Oliver & Waxman, 1986).

Bone pain, confined to single sites, usually responds to local external beam radiotherapy. Hemi-body irradiation can be used to control multifocal pain, but has the disadvantage of significant morbidity. An alternative approach is sequential treatments which often fail to obtain control of all painful sites and involve frequent

attendance at hospital. A further alternative approach to the relief of multifocal pain is to administer a radionuclide which concentrates at sites of increased bone turnover (Winston, 1979). Of the radionuclides tried, phosphorus-32 (Maxfield et al, 1958; Storaasli et al, 1961; Winston, 1979) has been used to the greatest extent, but without gaining general acceptance. Strontium-89 was first reported for pain palliation in 1942 (Pecher, 1942), but only recently have controlled studies been conducted (Robinson et al, 1987).

The aims of this study were to establish the efficacy of strontium-89 for the relief of metastatic bone pain and to estimate the optimum dose for patients with prostatic skeletal malignancy.

Physical properties and biodistribution of strontium-89

Strontium-89 is a pure beta-emitter (maximum beta energy 1.4 MeV) with a physical half-life of 51 days. Strontium follows the biochemical pathways of calcium in the body and is taken into the mineral structure of bone. It localizes preferentially at sites of increased mineral turnover, e.g. adjacent to metastatic deposits.

The biodistribution of strontium was investigated using strontium-85, a gamma-emitter which can be counted *in vivo*. The results (Blake et al, 1986; Blake et al, 1989) have been compared with previous studies of strontium metabolism in healthy subjects (ICRP, 1979). Strontium is cleared rapidly from the vascular compartment predominately by incorporation into bone mineral and excretion by glomerular filtration. Uptake is enhanced at sites of bone malignancy and retention at

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these sites is prolonged compared with normal bone, giving rise to an enhanced radiation dose absorbed by the lesions. Strontium whole body retention is a function of individual variations in urinary plasma clearance and metastatic load in the skeleton; between 12% and 90% of the administered activity is retained at 3 months (Blake et al, 1988).

Patients and methods

All patients entered in the study had bone metastases and pain in more than one site which no longer responded to conventional therapy. Prerequisites for entry in the study also included a life expectancy of at least 3 months, informed consent, adequate haematological function (leucocytes $> 3 \times 10^9 \text{ l}^{-1}$; platelets $> 100 \times 10^9 \text{ l}^{-1}$) and no change in systemic anti-cancer therapy over the preceding 3 months.

Strontium-89 chloride was provided by Amersham International and was given initially at a dose of 1.5 MBq/kg. The specific activity was in the range 3.3–5.0 MBq/mg elemental strontium and the strontium-90 content was $< 2 \times 10^{-4}\%$ at the reference date. Subsequently, patients entering the trial were given doses of 2.2 or 3.0 MBq/kg as part of an intended dose escalation study. When no change was observed in the pain relief obtained throughout the range 1.5–3.0 MBq/kg (see results below), some patients were treated with 0.7 MBq/kg.

At entry to the study a clinical examination was performed at which time a review of the patient's pain,

mobility and analgesic intake was made. A full blood count, biochemical profile and radionuclide bone image were obtained. The patient was asked to keep a diary recording pain levels at each site on a five point scale, analgesic intake, sleep pattern, appetite, mobility and mood for 7 days prior to treatment.

The strontium-89 was given by slow intravenous injection into an anti-cubital vein on an outpatient basis, no special radiological protection procedures being necessary.

After treatment patients continued to complete daily diaries. A full blood count and biochemical profile was obtained 2, 4, 6, 8, and 12 weeks post-therapy. Assessments at 4, 8 and 12 weeks were made and recorded on the form shown in Figure 1. The system was based on the experience of Robinson et al (1987) and took into account the patient's mobility and analgesic intake as well as the level of pain. A radionuclide bone image was repeated at the time of the final assessment at 12 weeks.

An arbitrary decision was taken to regard the assessment of response to treatment at 12 weeks as the main outcome in order to exclude, as far as possible, any placebo effects or short lived responses. Therefore, patients were considered non-evaluable if they died within the 3 month period, if they were lost to follow-up, or if alternative systemic therapy was commenced. However, patients receiving local field radiotherapy (e.g. for cord compression) were not removed, but the irradiated site was not included in the final assessment. It

General assessment

Please circle one of the assessments under each heading compared with the pre-administration examination on Form 3.

(a) General condition		(b) Mobility	
Deteriorated	–1	More restricted	–1
Unchanged	0	Essentially unchanged	0
Some improvement	+1	Less restricted	+1
Definitely better	+2		
(c) Analgesics		(d) Pain analysis	
Quantity increased	–1	At least 1 point increase in the majority of affected sites.	–2
Essentially unchanged	0	About 1 point increase in some sites.	–1
Quantity decreased by 20–45%	+1	No change in most sites.	0
Quantity decreased by 50–80%	+2	About 1 point decrease in some sites.	+1
Analgesics virtually discontinued	+3	At least 1 point decrease in the majority of affected sites.	+2

Overall assessment

Considering the above four assessments, assign the patient to one of the following five categories

	Guideline total of scores
1. Deteriorated	1. Negative
2. No significant change	2. –1/0/+1
3. Some improvement	3. +1/2/3
4. Substantial improvement	4. +4/5/6
5. Dramatic improvement	5. +7/8

Figure 1. Form used to record assessments at 4, 8 and 12 weeks.

Table I. 12 week assessment of patients with prostatic primaries treated with doses of strontium-89 of 1.5–3.0 MBq/kg

Dose in MBq/kg	1.5	2.2	3.0	Total
Died between 4 and 12 weeks	7	5	—	12
Unassessable	3	—	—	3
Dramatic improvement	13 (24%)	3 (18%)	2 (17%)	18 (22%)
Substantial improvement	19 (35%)	4 (24%)	4 (33%)	27 (33%)
Some improvement	9 (17%)	5 (29%)	3 (25%)	17 (20%)
No significant change	8 (15%)	2 (12%)	2 (17%)	12 (14%)
Deteriorated	5 (9%)	3 (18%)	1 (8%)	9 (11%)
Total assessable at 12 weeks	54	17	12	83

was determined that patients who showed evidence of response which was not maintained at the 12 week evaluation would be considered treatment failures.

The information obtained at 4 and 8 weeks in patients who did not survive 12 weeks is included in the results where it was available. However, it can be argued that responses which were sustained out to at least 12 weeks provide a better measure of the utility of the treatment.

Results

119 patients from four hospitals were entered in the study. Two patients had to be excluded as, owing to a misunderstanding between the relevant clinicians, alternative therapies were initiated a few days after the strontium injection was given. Another patient had to be ruled unassessable owing to a number of complications not associated with his prostatic disease. No follow-up information was obtained from nine patients, and a further nine patients died within 4 weeks of receiving their injections of strontium-89 and hence before the time of first assessment. At least some information was available on 98 patients and these results are recorded by dose and response in Table I. The table records the percentages of the patients assessable at 12 weeks showing each grade of response and it can be seen that of the total of 83 assessable patients 62 (75%) obtained a meaningful clinical response of which 18 (22%) became effectively pain free. It should be noted that these figures underestimate the total benefit received by the patients, since a few of those who did survive 12 weeks also obtained significant benefit from the treatment, but relapsed before their final assessment. No significant difference in response was seen at any dose level.

Information on the 15 patients who could not be assessed at 12 weeks is given in Table II. If we consider all 98 patients a clinical response at some time was noted in 70 (71%) of which 20 (20%) became effectively pain free.

Pain relief began typically between 10 and 20 days after strontium-89 administration, whilst maximum benefit was normally achieved by 6 weeks. Occasionally a slower response pattern was seen. Relief of pain was maintained for 4–15 months with a mean of 6 months.

A flare response was seen in some patients; this lasted 2–4 days and was generally an indicator of a good response.

At 12 weeks after treatment radionuclide bone images generally showed little change and there was no correlation between the change in bone image and clinical response. There was no correlation between changes in any of the biochemical parameters and clinical response. The only prognostic indicator of possible significance was the extent of bone metastases, some correlation between the bone image appearance at presentation and the response being seen in Table III.

The data in Table III was broken down further to see if there was any advantage in using higher doses within the range 1.5–3.0 MBq/kg in patients with more extensive skeletal metastases, but no such relationship was found.

In view of the fact that there was no obvious benefit

Table II. Outcomes on the 15 patients (Table I) not available for assessment at 12 weeks

Category	Number of patients	Outcomes
Died	2	Shown "dramatic improvement", ceased taking narcotics and died pain free.
	2	Shown "some improvement" at 4 weeks.
	1	Shown a good response at 4 weeks, but his pain returned prior to his death.
	5	Shown no significant change prior to death.
	2	Deteriorated prior to death.
Unassessable	1	Shown "substantial improvement" at 4 weeks, but was then lost to follow-up.
	2	Shown "some improvement" at 4 weeks, but deteriorated and received sufficient radiotherapy that they were considered unassessable.

Table III. Assessable patients treated with strontium-89 at doses of 1.5 MBq/kg and above categorized by response and extent of bone metastases

Response	Extent of metastases*			
	Light	Moderate	Extensive	Super-scan
Dramatic improvement	2 (22%)	6 (35%)	6 (14%)	4 (29%)
Substantial improvement	5 (55%)	7 (41%)	12 (28%)	3 (21%)
Some improvement	1 (11%)	3 (18%)	11 (26%)	2 (14%)
No change	1 (11%)	1 (6%)	8 (19%)	2 (14%)
Deteriorated	—	—	6 (14%)	3 (21%)

*The extent of metastases was measured in a controlled fashion from skeletal images following injection with $^{99}\text{Tc}^{\text{m}}$ -MDP. Scores were converted into the four groupings named above.

Table IV. Cumulative mortality of patients at various times after treatment with various doses of strontium-89

^{89}Sr dose (MBq/kg)	Patients treated	Patients lost (survival unknown)	Numbers dead by end of:—		
			4 weeks	8 weeks	12 weeks
0.7	11	1	—	1 (10%)	2 (20%)
1.5	78	3	6 (8%)	11 (15%)	15 (20%)
2.2	27	1	2 (8%)	7 (27%)	8 (31%)
3.0	14	—	1 (7%)	1 (7%)	1 (7%)

Figures in parentheses give the cumulative mortality at the various times, expressed as a percentage of the patients at risk.

obtained by increasing the dose between 1.5 and 3.0 MBq/kg a further 11 patients were treated with 0.7 MBq/kg. Five patients were evaluable at 12 weeks, of which one showed "some improvement" and the rest showed no change.

No immediate adverse reactions to the administration of strontium-89 were observed and no differences in cumulative mortality between the groups receiving different doses were seen (Table IV). A fall in platelet levels was seen in most patients, with the nadir occurring about 6 weeks after treatment. There is a significant ($p < 0.02$) increase in the mean percentage depression with increasing doses of strontium-89 (Table V). However, no patient treated with strontium-89 showed WHO Grade III haematological toxicity (platelets $< 50 \times 10^9 \text{ l}^{-1}$ or leucocytes $< 2 \times 10^9 \text{ l}^{-1}$) up to 6 weeks post-therapy. In patients surviving the 12 weeks of the study there was no correlation between the extent of skeletal metastases and the depression of platelet levels following the administration of strontium-89.

Table V. Mean percentage depression in platelet levels from all patients for whom data was available at six weeks post treatment with various doses of strontium-89

Dose (MBq/kg)	Patients	Percentage depression
0.7	6	19%
1.5	57	24%
2.2	17	28%
3.0	11	45%

24 patients were retreated for recurrence of pain; 18 received two injections of strontium-89, five received three injections and one received four injections. In all but one case the same dose of strontium-89 was used for successive treatments as was used for the initial treatment. The response to the additional treatments was generally comparable with that seen in the first treatment for an individual patient. The fall in platelet count tended to be by the same percentage of baseline values as was seen after the first treatment. Figure 2 illustrates changes in platelet and leucocyte count in a patient treated on four occasions over a 3 year period.

Discussion

Strontium-89 relieves bone pain in the majority of symptomatic patients with prostatic malignancy even when those patients have failed conventional therapies. At 12 weeks after treatment with a dose of at least 1.5 MBq/kg 75% of assessable patients obtained some control of symptoms and more than 20% had become essentially free of pain. The results are similar to earlier reports by Robinson et al (1987). Additionally, as noted above, there were a few cases of patients obtaining significant benefit, but relapsing by 12 weeks, and hence being classed as treatment failures. Some of the patients who failed to survive 12 weeks also appeared to obtain real benefit from the treatment.

One objective of this study was to see if there was an optimal dose of strontium-89 for pain relief. From the results recorded in Table IV it is clear that mortality is not dose related. Additionally, there is no evidence that haematological toxicity is a major problem, although

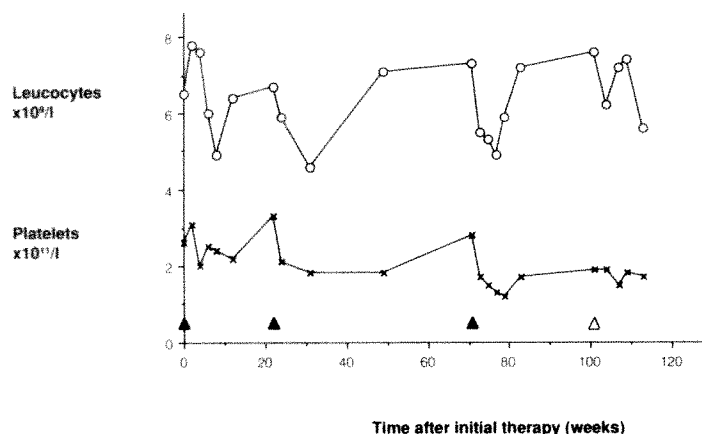


Figure 2. Leucocyte and platelet levels for the patient who received the greatest total dose of strontium-89 chloride.

—○— leucocytes; —×— platelets;
▲ strontium-89 therapy at 2.2 MBq/kg;
△ strontium-89 therapy at 1.1 MBq/kg.
Patient died in 156th week after initial strontium-89 therapy.

the expected trend is observed and hence it is desirable to choose the lowest effective dose. From the results in Table I, we appeared to have a plateau of response over the dose range 1.5–3.0 MBq/kg. The possibility that this apparent lack of dose response was caused by pooling results from patients with different extents of skeletal involvement was examined, but found not to be the case. A combination of our results (omitting those from Edmonton where the dose of 1.5 MBq/kg was used throughout) with those from other studies conducted in the USA under the auspices of Amersham International, and reported in abstract form (Lamki et al, 1989; Robinson et al, 1989), are given in Table VI.

These results strongly indicate that doses below 1.5 MBq/kg are suboptimal for pain relief, but they also suggest that, in general, doses above 1.5 MBq/kg offer little additional benefit. Accordingly a standard dose of 150 MBq for each patient is recommended as offering optimal pain relief. The limited extent of the dose response was unexpected, but it is noteworthy that several authors report that pain relief may be achieved by local field radiotherapy at radiation doses significantly lower than those conventionally used for tumour control (Vargha et al, 1969; Allen et al, 1976; Jensen & Roesdahl, 1976; Gilbert et al, 1977; Tong et al, 1982; Price et al, 1986, 1988) and at least four publications (Vargha et al, 1969; Allen et al, 1976; Jensen &

Roesdahl, 1976; Tong et al, 1982) refer to a lack of dose response.

Whilst, as mentioned above, serious toxicity is virtually always a result of the patient's disease, some depression of platelets following the administration of strontium-89 is observed. The figures in Table V represent a summation of the effects of the disease process and radiation from strontium-89, but the correlation with dose is significant ($p < 0.02$). The average depression to be expected at the recommended dose is about 30% and this normally should present no clinical problems, especially as recovery typically will occur over the ensuing 3 or 4 months. However, it indicates that patients being treated with strontium-89 should undergo regular haematological monitoring.

One of the patients treated at 0.7 MBq/kg could not be assessed because he was found to have been receiving calcium medication and this was reflected in an exceptionally poor uptake of strontium following his treatment. Evidently patients should discontinue such medication at least 2 weeks before being treated with strontium-89.

Experience with repeat strontium-89 therapy is limited, but some tentative conclusions may be drawn. Patients may be retreated safely at the recommended dose at intervals of 3 months or more if pain recurs. However, the peripheral blood count must be acceptable. Patients who failed to respond to their first strontium-89 injection are unlikely to benefit from retreatments.

There was no obvious prognostic factor as to which patients benefitted most from this therapy. Particular attention was paid to the extent of bone metastases. Although our results did not indicate that higher doses were required for patients with more extensive metastatic involvement of the skeleton, there was some indication that better results were obtained in patients with fewer metastases. However, that must be qualified by noting that 50% of super-scan patients showed either a substantial or a dramatic improvement. It appears, therefore, that there may be an advantage in using strontium-89 at an early stage of metastatic skeletal

Table VI. Summary of US/UK dose ranging studies on strontium-89

Response at 12 weeks	Patients receiving stated dose (MBq/kg)			
	0.7–0.9	1.5	2.0–2.2	2.6–3.1
Dramatic/substantial improvement	2 (17%)	25 (68%)	12 (44%)	16 (55%)
Some improvement	2 (17%)	6 (16%)	9 (33%)	8 (28%)
No change/worse	8 (67%)	6 (16%)	6 (22%)	5 (17%)
Total assessable patients	12	37	27	29

disease. However, no patient who fulfills our trial criteria should be excluded because of the extensive nature of his skeletal disease.

The encouraging results obtained using strontium-89 warrant comparison with alternative palliative treatments. Hemi-body radiotherapy has been used to relieve multifocal pain, but its benefit must be weighed against significant morbidity (Rowland, 1979; Salazar et al, 1981). By comparison, strontium-89 therapy is well tolerated and is repeatable. Radionuclides other than strontium-89 may be of value (Harbert, 1987). Phosphorus-32 was used for many years, but was generally felt to give rise to unacceptable marrow toxicity (Maxfield et al, 1958; Storaasli et al, 1961; Winston, 1979). More recent studies with phosphorus-32 (Glaser et al, 1981; Burnet et al, 1990) have claimed no significant haematological effects and a response rate of over 80%, but the treatment protocol involved androgen priming and a period of inpatient care. Moreover, there was no evidence as to the period of pain remission and the response rate may have included some cases showing transient responses. Iodine-131 (Eisenhut et al, 1986), samarium-153 (Corwin et al, 1988) and rhenium-186 (Soldano et al, 1988) conjugates have been tried and a recent report (Turner et al, 1989) suggests that samarium-153 might give earlier clinical responses than typically seen with strontium-89, but that such responses are of shorter duration. Direct clinical comparisons would be needed to establish such apparent differences, but from the relative half-lives of the radionuclides they would not be unexpected. Overall these conjugates do not seem to offer significant advantages over strontium-89.

Further research to compare strontium-89 treatment with hemi-body and local field radiotherapy is in progress. Following the suggestion that strontium-89 therapy increases survival (Buchali et al, 1988), its role as an adjunct to local radiotherapy is also being evaluated.

Environmental considerations

As strontium-89 is a pure beta-emitter the treated patient poses no direct radiation risk to other people. Treatment of incontinent patients is evidently contra-indicated; otherwise normal toilet facilities suffice for the disposal of excreted activity, but patients should use water closets rather than urinals for the first week after treatment.

Calculations by the National Radiological Protection Board (Cooper et al, 1989) have shown that there is no hazard to crematorium operators, or other members of the public, as a consequence of cremating corpses containing up to 500 MBq of strontium-89. This level greatly exceeds that used for pain palliation. Related calculations by the Board (Cooper et al, 1989) showed that, postulating the most widespread use of strontium-89 imaginable, the contribution to the radiological dose received by the general public as a consequence of environmental contamination would be significantly below one thousandth of the average natural background in the British Isles.

It should be noted that the amount of the long-lived radionuclide strontium-90 in the strontium-89 utilized is less than $2 \times 10^{-4}\%$ at reference date.

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The relative biological effectiveness of fractionated doses of fast neutrons ($42 \text{ MeV}_{d \rightarrow \text{Be}}$) for normal tissues in the pig

IV. Effects on renal function

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Abstract. The effects of fractionated doses of fast neutrons ($42 \text{ MeV}_{d \rightarrow \text{Be}}$) on the radiation response of the pig kidney have been assessed and compared with those observed after X irradiation. Following X irradiation there was a marked increase in the total dose at which renal function was preserved with decreasing fraction size. The rate of this increase was dependent on the overall treatment time; for fractionated irradiation given over 18 or 39 days the exponents related to fraction number, N , were 0.36 ± 0.03 and 0.48 ± 0.003 , respectively. In contrast, there was no significant change in the iso-effect dose for renal injury following fractionated irradiation with fast neutrons where there was also little effect of varying the overall treatment time. Analysing these data by means of the linear-quadratic (LQ) model, using both an Fe-plot and the Tucker test, gave α/β ratios of $2.42 \pm 0.06 \text{ Gy}$ and $2.99 \pm 0.16 \text{ Gy}$, respectively, for X-ray doses given in 18 days. For fractionated doses of X rays given in 39 days the α/β ratios were $0.40 \pm 0.01 \text{ Gy}$ and $0.47 \pm 0.02 \text{ Gy}$, respectively. The α/β ratios for renal tissue following fast neutron irradiation obtained by the two methods were also similar, *i.e.* $15.00 \pm 0.60 \text{ Gy}$ and $15.72 \pm 3.76 \text{ Gy}$, respectively. The pronounced fractionation effect seen with X irradiation, particularly for doses administered over 39 days as opposed to 18 days, coupled with the absence of any such effect with fast neutrons, resulted in a marked increase in relative biological effectiveness (RBE) with decreasing X-ray dose/fraction. The slopes of the resulting regression lines were -0.73 ± 0.05 and -0.33 ± 0.02 , respectively. The lack of dose sparing associated with fractionation, or variation of the overall treatment time for fast neutron irradiation, suggests that doses administered to tumours adjacent to the kidney can be given as a few relatively large dose/fractions in a short overall treatment time without an increased risk of complications related to renal tissue. This may be of therapeutic advantage in the treatment of rapidly proliferating tumours where dose may be wasted using more conventional protracted fractionated irradiation schedules.

A major limitation of the neutron beams used in the earlier clinical trials of neutron therapy (Catterall et al, 1975; Pointon et al, 1985; Duncan et al, 1986) were the poor depth-dose characteristics of the beams produced by 16 MeV deuterons on a beryllium target. To overcome this problem a second generation of higher cyclotrons has been developed. Neutron beams produced by the bombardment of a beryllium target with either higher energy deuterons or photons have depth-dose characteristics similar to ^{60}Co γ rays or 4 MeV X rays (Catterall & Bewley, 1979). In the UK a clinical high energy neutron facility ($62 \text{ MeV}_{p \rightarrow \text{Be}}$) has been provided by the installation of a cyclotron at the Clatterbridge Hospital, Merseyside. In order to obtain radiobiological data for higher energy neutrons, a neutron beam line was constructed based on the Variable Energy Cyclotron (VEC) at the Atomic Energy Research Establishment (AERE), Harwell. This produced fast neutrons with an average energy of 14 MeV (Goodhead et al, 1977). Using this neutron beam an extensive experimental study has been carried out, in a large animal model, to investigate the variation in RBE with dose fractionation, specifically for late radiation effects on normal tissues. The use of a large animal, *i.e.* the pig,

has several advantages in that tissue volumes comparable with those used clinically can be irradiated. Thus dose distributions similar to those obtained clinically are used. In addition, the pig exhibits a number of physiological similarities to that of Man; in terms of the kidney the pig is unique among laboratory animals in possessing a multipapillate, multipyramidal kidney similar to that of Man (Sperber, 1944). There are other functional and biochemical similarities between the kidneys of the two species (Terry, 1986; Livio et al, 1988). Thus the results of studies on the pig are more likely to have direct clinical relevance.

In this paper the effects of fast neutron irradiation are compared with those for X irradiation (250 kV) for late changes in renal function. Investigations related to early and late effects in skin and subcutaneous tissues (Hopewell et al, 1988, 1990), the lung (Rezvani et al, 1990) and rectum have already been published or are being prepared for publication.

Materials and methods

A total of 111 female pigs of the Large White strain were used in these investigations. Of these 77 were irradiated with fast neutrons and the remaining animals

were exposed to 250 kV X rays. The animals were brought into the animal house when they were approximately 12 weeks of age (20–25 kg body weight) and were allowed an acclimatization period of at least 2 weeks before any experimental procedures were undertaken. All procedures were carried out under anaesthesia using 2% halothane, ~70% oxygen and ~30% nitrous oxide gas mixture (Dickinson & Hubbard, 1990).

Prior to irradiation the position of each kidney was determined by intravenous pyelography and the position of the right kidney included in an 8 cm × 12 cm field tattooed on the overlying skin. Neutron irradiations were carried out using the VEC at the AERE. The physical characteristics of this beam have been described in detail previously (Goodhead et al, 1977). Neutrons were produced by the bombardment of a 2 mm thick gold-backed beryllium target with 42 MeV deuterons. The target to skin distance was 150 cm, giving a dose rate of 0.45–0.5 Gy/min. The right kidney was irradiated with single doses of fast neutrons or as total doses given as 6 or 12 fractions in 18 days and as 6, 12 or 30 fractions in 39 days. For each fractionation schedule 5–6 dose levels were used; each dose group contained 1–4 animals. Photon irradiations were carried out using 250 kV X rays, half-value layer (HVL) 1.4 mm Cu (Hopewell & Berry, 1974) at a dose rate of ~0.5 Gy/min to the midline of the kidney. In addition to a Perspex ended applicator (focus-skin distance (FSD) 50 cm), the irradiation field was further delimited by an 8 cm × 12 cm cut-out in 3 mm lead placed on the skin surface overlying the right kidney. X rays were given as a single dose, as 6 or 14 fractions in 18 days and as 6, 12, 14, 18 or 30 fractions in 39 days. The majority of the results obtained for X rays have been published previously (Hopewell & Berry, 1974, 1975; Hopewell & Wiernik, 1977; Robbins & Hopewell, 1987).

Prior to irradiation, and at regular intervals from 4–104 weeks after irradiation, renal function was assessed by probe-renalography. Following fractionated irradiation all investigations were timed relative to the midpoint of the schedule. In the initial stages of this study renal function was assessed semiquantitatively using ¹³¹I-hippuran renalography (Hopewell & Berry, 1974). This was later replaced by more quantitative methods of measuring renal function, details of which have been reported previously (Robbins et al, 1984). Briefly, three matched NaI scintillation detectors were used, one positioned over each kidney and the other over the heart. The detectors were connected to a multi-

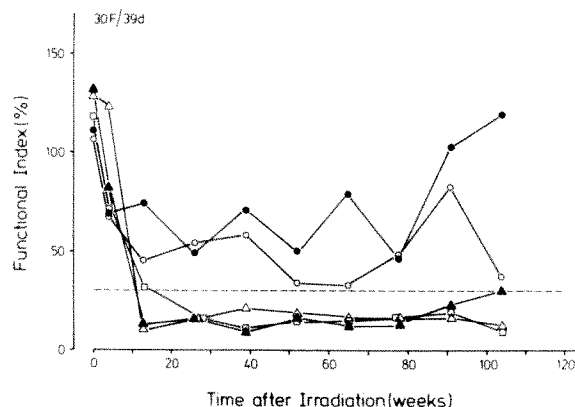


Figure 1. Time-related changes in the mean functional index of kidneys irradiated with 30 fractions of fast neutrons (42 MeV_{d-Bec}) given in 39 days (● 7.2 Gy; ○ 8.2 Gy; ▲ 9.2 Gy; △ 10.2 Gy; □ 12.2 Gy). The points beneath the dotted line (FI < 30%) represent non-functioning kidneys.

channel analyser set to record the activity in the photopeak region for ¹³¹I. The analyser was operated in the multiscaling mode to provide counts, from each detector, integrated over 20 s intervals for the duration of each renogram. The tracer ¹³¹I-hippuran (1.85–12.95 MBq, depending on the size of the pig) was used to provide an estimate of effective renal plasma flow (ERPF). The tracer was injected via an ear vein and the time-related changes in activity over each kidney and the heart were recorded for up to 40 min. Simultaneous estimates were also made of the glomerular filtration rate (GFR) using the tracer ^{99m}Tc-DTPA (Robbins et al, 1984). A detailed report of changes in GFR and ERPF, induced by fast neutrons, will be published elsewhere (Robbins et al, in preparation).

Function in the irradiated kidney was compared with that in the contralateral unirradiated kidney to establish a functional index (FI). In the initial semiquantitative assessment (Hopewell & Berry, 1974) the FI was estimated from the ratio of the peak height of the renogram for the irradiated kidney to that observed in the contralateral unirradiated kidney in the same animal. With the development of a more quantitative technique, the FI was estimated from the ratio of the uptake function of ¹³¹I-hippuran in the irradiated kidney compared with that obtained from the unirradiated kidney in the same animal. Three levels of function were defined from the values of the FI (Table I). Irradiated kidneys in which the FI was <30% were defined as having "no significant function". RBE values were calculated either on the basis of the maximum dose at which function was still preserved, the minimum dose at which "no significant function" was observed, or the intermediate "iso-effect dose" midway between these two effect levels. These doses were, in general, calculated for FI values measured 104 weeks after irradiation, although in some cases earlier time intervals were used owing to the premature loss of animals.

Table I. Shows arbitrary subdivision of the results of renograms into three levels of effect based on the value of the functional index (FI)

FI (%)	Classification
72–138	Normal function (F)
30–72	Reduced function (RF)
<30	No significant function (NF)

Results

An example of the time-related changes in the value of the mean FI observed following irradiation of pig kidneys with fast neutrons is illustrated in Fig. 1. This figure shows the FI results for kidneys irradiated with 30 fractions of fast neutrons given over 39 days. The changes in the FI, classified in terms of the three levels of function defined in Table I, are listed in Table II for animals irradiated with 30F/39 days of fast neutrons or X rays. These results indicate that for this fractionation schedule of fast neutrons, functioning and non-functioning kidneys were associated with total doses of 8.2 Gy and 9.2 Gy, respectively. Thus the "iso-effect dose" for this fractionation schedule was estimated to be 8.7 Gy. These iso-effect doses and those for other fractionation schedules for the radiation response of the pig kidney to X irradiation and fast neutron irradiation are given in Table III. These results indicate that following X irradiation there was a marked increase in the iso-effect dose with increasing fraction number, and hence decreasing fraction size, particularly for fractionated doses given over 39 days. In contrast, there was no significant increase in the iso-effect dose between 6 and 30 fractions after fast neutron irradiation (Table III).

A log-log plot of the "intermediate" iso-effect dose against fraction number indicated that the steepness of the iso-effect plot was clearly dependent on the overall treatment time over which fractionation of the total radiation dose was given (Fig. 2). Thus for X-ray doses given as 6 and 14 fractions over 18 days a line could be fitted with a slope equivalent to an N exponent of 0.36 ± 0.03 , compared with a significantly steeper ($p < 0.001$) slope of 0.48 ± 0.003 for fractions given in

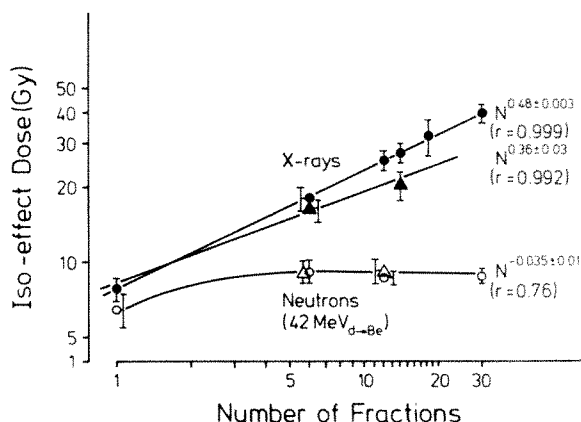


Figure 2. Log-log plot of iso-effect doses for pig kidney damage against the number of fractions of X rays (●, ▲) or fast neutrons (42 MeV_{d-Bc}) (○, △). Irradiation was given in 18 (△, ▲) or 39 days (○, ●). Bars represent the range of dose between the maximum dose at which renal function was preserved and the minimum dose at which no significant function was observed.

39 days. In both cases the single dose result was included in the regression line fit.

In contrast to the results for X rays, there was no significant increase in iso-effect dose with increasing fraction number following fractionated irradiation with fast neutrons (Fig. 2). However, there was an ~60% increase in the iso-effect dose when doses given in 6 fractions were compared with the single dose result. On

Table II. The time-related changes in values of the functional index for the kidney of the pig following irradiation given as 30 fractions over 39 days

Radiation	Total dose (Gy)	Pig number	Time after irradiation (weeks)								
			4	13	26	39	52	65	78	91	104
250 kV X rays	17.2	114	F	F	F	F	F	F	F	F	F
	23.7	113	F	F	RF	F	RF	F	F	F+	F
	30.2	59	F	RF	RF	NF	F	RF	NF	NF	RF
	36.4	58	F	RF	F	RF	RF	NF	NF	NF	RF
	43.1	72	F	—	NF	NF	NF+				
	49.5	73	F	RF	NF	NF	NF+				
Fast neutrons 42 MeV _{d-Bc}	7.2	83	F	F	RF+						
	7.2	86	F	F	F	F	RF	F+			
	7.2	136	F	F	RF	F	RF	F	RF	F	F
	7.2	137	F	F	F	RF+					
	8.2	39	F	F	F	F	F	NF	F	F	F
	8.2	84	RF	RF	F	NF	NF	NF	RF	F	RF
	8.2	134	RF	RF	RF	RF+					
	8.2	135	RF	RF	RF	RF	RF	RF	RF	F	—
	9.2	85	F	NF	NF	NF	NF	NF	NF	NF+	
	9.2	87	RF	NF	NF	NF	NF	NF	NF	NF	RF
	10.2	78	F	NF	NF	NF	NF	NF	NF	NF	NF
	12.2	44	F	NF	NF	NF	NF	NF	NF	NF+	

F = Normal function; RF = reduced function; NF = no significant function.

+ Denotes death of animal.

a log-log plot of iso-effect dose against the number of fractions of fast neutrons a regression line, fitted between 6 and 30 fractions, suggested an N exponent of -0.035 ± 0.01 ; this was not significantly different from zero. There was no significant change in the response by varying the overall treatment time.

Assuming the applicability of the LQ model, these data were further analysed by plotting the reciprocal of the iso-effect dose *versus* the respective X-ray and fast neutron dose/fraction (Fig. 3). From the results of studies with X rays it was possible to resolve two different values for the α/β ratio, depending on the overall treatment time. For X irradiation given in 18 days the α/β ratio was 2.42 ± 0.06 Gy; this was significantly higher ($p < 0.001$) than the value of 0.40 ± 0.01 Gy, obtained from the data for X irradiation given over 39 days. The results from the fast neutron data were all well fitted to a single line, indicating an α/β ratio of 15.00 ± 0.60 Gy. The α/β ratios were also determined using the method proposed by Tucker (1984); the values obtained using this method were similar to those derived from the reciprocal iso-effect

dose plots. For X rays given in 18 days the α/β ratio was 2.99 ± 0.16 Gy, which was significantly larger ($p < 0.001$) than the value of 0.47 ± 0.02 Gy obtained for X irradiation given over 39 days. It should be recognized that the latter α/β ratio was obtained by forcing the regression line through the origin on a Tucker plot, indicating that the LQ model did not appear to describe the dose fractionation response adequately for X rays when given over 39 days. A similar analysis of the fast neutron results gave an α/β ratio of 15.72 ± 3.76 Gy.

The RBE values determined for the various fractionation schedules are listed in Table III; in general the RBE increased with increasing fraction number and hence decreasing fraction size. For convenience a log-log plot of the variation in RBE value against the X-ray doses/fraction was used. This showed that variation was also dependent on overall treatment time (Fig. 4). For fractionated irradiation, given over 18 days, the data were well fitted by a regression line with a slope of -0.33 ± 0.02 ; a significantly steeper ($p < 0.001$) slope of -0.73 ± 0.05 was obtained for X-ray doses/fraction given over a 39 day period. For clinically relevant doses/

Table III. Iso-effect doses and RBE values for renal damage in the pig after X-ray and fast neutron (42 MeV_{d-Bc}) irradiation

Fractionation (fractions/days)	Effect level	Dose (Gy) required to produce a given effect		
		X rays	Neutrons	RBE
Single dose	F	7.0 (7.0)	5.50 (5.5)	1.27
	IE	7.9 (7.9)	6.50 (6.5)	1.22
	NF	8.8 (8.8)	7.50 (7.5)	1.17
6/39	F	15.95 (2.66)	8.20 (1.37)	1.95
	IE	18.12 (3.02)	9.20 (1.53)	1.97
	NF	20.29 (3.38)	10.20 (1.70)	1.99
12/39	F	23.40 (1.95)	8.20 (0.68)	2.85
	IE	25.50 (2.13)	8.70 (0.73)	2.93
	NF	27.60 (2.30)	9.20 (0.77)	3.00
14/39	F	25.00 (1.79)	—	—
	IE	27.50 (1.96)	—	—
	NF	30.00 (2.14)	—	—
18/39	F	26.30 (1.46)	—	—
	IE	31.95 (1.78)	—	—
	NF	37.60 (2.09)	—	—
30/39	F	36.40 (1.21)	8.20 (0.27)	4.44
	IE	39.75 (1.33)	8.70 (0.29)	4.57
	NF	43.10 (1.44)	9.20 (0.31)	4.69
6/18	F	14.56 (2.43)	8.20 (1.37)	1.78
	IE	16.56 (2.76)	9.20 (1.53)	1.80
	NF	18.57 (3.10)	10.20 (1.70)	1.82
12/18	F	—	8.20 (0.68)	—
	IE	*19.00 (1.58)	9.20 (0.77)	2.07
	NF	—	10.20 (0.85)	—
14/18	F	17.93 (1.28)	—	—
	IE	20.38 (1.46)	—	—
	NF	22.83 (1.63)	—	—

*Estimated by extrapolation from existing 250 kV X-ray data.

F = Maximum dose at which function was preserved; IE = intermediate iso-effect dose; NF = minimum dose at which function was lost.

Figures in parentheses refer to dose per fraction.

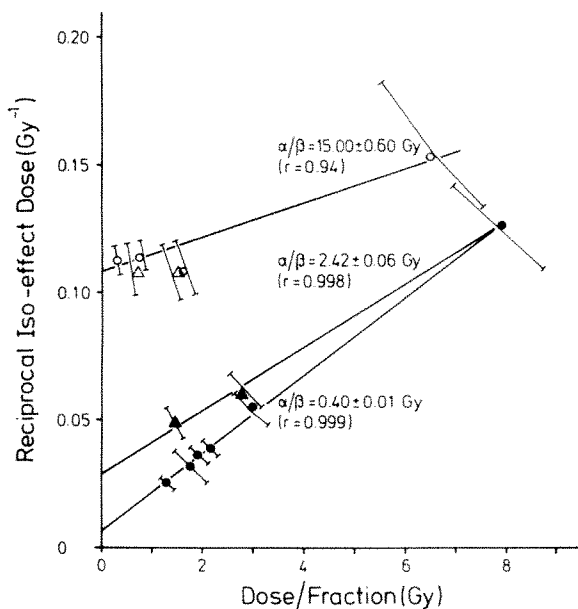


Figure 3. Plot of the reciprocal iso-effect doses for radiation damage to the pig kidney as a function of the dose per fraction of X rays or fast neutrons (42 MeV_{d-Bc}). (For key to symbols see Fig. 2.)

fraction of ~ 2 Gy, the RBE for renal damage varied between 2.0 and 3.0 for fast neutrons (42 MeV_{d-Bc}) as compared with 250 kV X rays depending on the overall treatment time.

Discussion

The present findings, concerning the variation in iso-effect dose for renal radiation damage following fractionated irradiation with X rays, clearly indicate that the size of the dose/fraction markedly influences the total dose at which renal function is preserved. However, the extent of this increase in total dose varies depending on the overall treatment time. Thus, for fractionated X irradiation given over 18 days an N exponent of 0.36 ± 0.03 was obtained, whereas for fractionated X irradiation given over 39 days a significantly higher value ($p < 0.001$) of 0.48 ± 0.003 was observed. In both cases the data showed an excellent fit on the basis of linear regression analysis. In a previous report, of the response of the pig kidney to fractionated irradiation with X rays (Hopewell & Berry, 1975), N exponents of 0.24 and 0.49 had been quoted for fractionated irradiation given in 18 and 39 days, respectively. These analyses did not include the single iso-effect dose of 10.7 Gy determined from the semi-quantitative analysis of the ^{131}I -hippuran renogram (Hopewell & Berry, 1974). More recent studies utilizing a more precise quantitative analysis of the renogram and a greater number of animals (Robbins et al, 1984) have indicated that the intermediate iso-effect dose following irradiation with single doses of X rays is

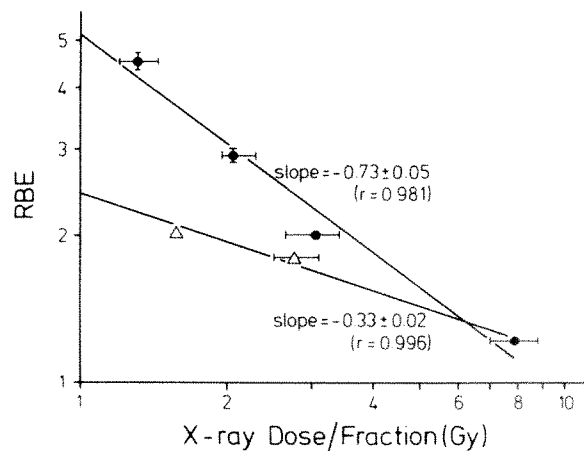


Figure 4. Log-log plot of the variation in RBE values for pig kidney damage against the X-ray dose/fraction for overall treatment times of 18 (Δ) or 39 days ($\bullet$). Bars represent the range of RBE values and X-ray doses/fraction obtained by comparing the maximum dose of fast neutrons (42 MeV_{d-Bc}) and X rays at which function was preserved, and the minimum dose at which there was no significant function.

7.9 Gy (Robbins & Hopewell, 1988). Incorporating this revised data point into the analysis, along with the results for fractionation given as 12, 14, 18 and 30 fractions, had no significant effect on the value of the N exponent for X-ray doses given over 39 days. However, inclusion of the single dose result did result in an increase in the value of the N exponent for X irradiation given over 18 days, i.e. 0.36. However, these results still indicated a larger value for the N exponent for X-ray doses/fraction administered over 39 days as compared with those given over 18 days.

It is of interest to compare the present results following renal irradiation with those obtained following X irradiation of other normal tissues in the pig. For both the acute response of the skin, i.e. moist desquamation (Hopewell et al, 1988) and the early response of the lung, i.e. radiation pneumonitis assessed between 13 and 39 weeks after irradiation (Rezvani & Hopewell, 1990), there was an increase in the iso-effect dose for 6 fractions given in 39 days as compared with 18 days. However, no significant increase was seen for 14 fractions given in 39 days as compared with 14 fractions in 18 days. This contrasts with present findings for the kidney and also those for late dermal necrosis in pig skin (Hopewell & van den Aardweg, 1991) where there was an increase in the iso-effect dose for irradiation given as 14 fractions when the overall treatment time was increased from 18 to 39 days.

In the case of late dermal necrosis the result was interpreted as indicating the presence of some incomplete repair even with interfraction intervals of 24 h (Hopewell & van den Aardweg, 1991). An increase in the size of the N exponent, with increased overall treatment time, has also been reported for the kidney by

other investigators using different experimental systems. Williams and Denekamp (1984) obtained an N exponent of 0.42 for doses given as 2 to 16 fractions delivered over 35 to 40 days, whilst for 2 and 5 fractions delivered in 4 days the N exponent was only 0.33, a result broadly in agreement with the present findings. Glatstein et al (1975) also reported low values for the N exponent of 0.21 and 0.27 for irradiation given over 4 and 9 days, respectively. In an additional study in mice (Stewart et al, 1984a), up to 64 fractions of X rays of between 0.9 and 16 Gy/fraction were given in 21 days. For up to 16 fractions the N exponent was found to be 0.42 and for >16 fractions the value of N was reduced to 0.24, an effect that has been attributed, at least in part, to the incomplete repair of sublethal damage (SLD) when 2 fractions/day were given with relative short interfraction intervals (Thames et al, 1988). These results also suggested that the repair of SLD was incomplete within 24 h. Indeed, later studies (Stewart et al, 1987) involving X irradiation given as 40, 60, or 80 fractions and given with an interfraction interval of 5 h, resulted in lower than predicted iso-effect doses. Thus such a short interfraction interval appears insufficient to allow the full repair of SLD. For some acutely responding normal tissues SLD repair may be almost complete within 3 h for small doses per fraction (Withers et al, 1975; Ang et al, 1985). However, repair half-times (T_1) for late responding tissues, such as the spinal cord and dermis, could be of the order of at least 2 h (Ang et al, 1987; Hopewell & van den Aardweg, 1989). In the kidney a T_1 value of 2.1 h has been reported to be characteristic of late reactions for small doses per fraction (van Rongen et al, 1990). These latter findings further support the hypothesis that interfraction intervals of ≤ 24 h are associated with the incomplete repair of SLD, and hence a reduction in the anticipated iso-effect dose.

In contrast to the marked variation in iso-effect dose following fractionated irradiation with X rays, there was no significant change in the iso-effect dose for renal injury following fractionated irradiation with fast neutrons. There was also no effect of changing the overall treatment time. A similar lack of a fractionation effect has been observed in other studies following kidney irradiation with fast neutrons (Stewart et al, 1984b; Joiner & Johns, 1987) and in other late responding normal tissues (Withers et al, 1982; Hopewell et al, 1990; Rezvani et al, 1990).

As discussed earlier, based on the results of studies in the mouse (Stewart et al, 1984a), the size of the N exponent appeared to decline as a function of fraction number. This would be expected if the underlying cell survival curves for the target cell(s) responsible for the development of renal damage were consistent with the LQ model. In general, experimental data based on the results of functional studies following photon irradiation of the kidney have been well described by the LQ model; α/β ratios were in the order of 2–3 Gy (Williams & Denekamp, 1984; Stewart et al, 1987), although lower values of approximately 1.7 have been reported recently (van Rongen et al, 1990). For the pig kidney data it was

possible, using either a Fe-plot (Douglas & Fowler, 1976) or Tucker's test (Tucker, 1984), to resolve two values of the α/β ratios depending on the overall treatment time. For X irradiation given over 18 days the α/β ratios obtained were 2.42 ± 0.06 Gy and 2.99 ± 0.16 Gy, respectively. These values were similar to the α/β ratio of 2.17 ± 0.33 Gy reported by Joiner (1989) following the X irradiation of the mouse kidney in an overall treatment time of approximately 3 weeks. However, for fractionated doses of X rays given in 39 days, α/β ratios of 0.40 ± 0.01 Gy and 0.47 ± 0.02 Gy, respectively, were obtained. The reason(s) for these very low α/β ratios remain unclear. It should be noted that using Tucker's test it was found that the data could not be adequately defined by the LQ model. However, similar low values for the α/β ratio have been obtained for low doses/fraction in the pig lung (Rezvani et al, 1990) and for both early and late damage in pig skin when full allowance was made for incomplete repair after doses/fraction of ≤ 7 Gy (Hopewell & van den Aardweg, 1991).

Data for the pig kidney following fast neutron irradiation seemed to be well described by the LQ model. This confirms earlier observations (Stewart et al, 1984b; Joiner & Johns, 1987). The α/β ratio obtained from the Fe-plot was 15.00 ± 0.60 Gy, a value not significantly different from the value of 15.72 ± 3.76 Gy derived using Tucker's test. Similarly high α/β ratios have been reported for the mouse kidney (Stewart et al, 1984b; Joiner & Johns, 1987) and other normal tissues (Withers et al, 1982; Hopewell et al, 1988, 1990; Rezvani et al, 1990) following fast neutron irradiation.

The pronounced fractionation effect seen with X irradiation, particularly over 6 as opposed to 3 weeks overall treatment time, coupled with the lack of any such effect with fast neutrons, resulted in a marked increase in RBE with increasing fraction number or decreasing fraction size. For a treatment time of 18 days the slope of the regression line was -0.33 ± 0.02 . For a treatment time of 39 days the slope of the regression line was -0.73 ± 0.05 . These results indicate that for clinically relevant doses of ~ 2 Gy/fraction the RBE was 1.9 and 3.1, respectively. Joiner (1989) reported that for a similar X-ray dose/fraction the best estimate of the RBE for renal damage in the mouse was 3.1 when using p(62)-Be neutrons and 4.5 for d(16)Be neutrons. The latter much higher RBE value reflects the differences in the energy of the different neutron beams (Hall et al, 1975; Kellerer et al, 1976). The RBE value of ~ 3 , obtained for the pig kidney following X-ray doses/fraction of ~ 2 Gy given over 39 days, is similar to that previously reported for the pig lung (Rezvani et al, 1990) and for dermal and subcutaneous tissues (Hopewell et al, 1988, 1990). In these tissues there was also no evidence for any effect of a change in overall treatment time.

The findings presented here indicate a marked increase in RBE with decreasing dose/fraction for the kidney, with little evidence of any sparing resulting from fractionation or varying the overall treatment time for

fast neutron irradiation. In terms of their clinical use these data suggest that fast neutrons can be given just as safely to the kidney as a few relatively large fractions in a short overall treatment time. This would be likely to be of therapeutic advantage in the treatment of rapidly proliferating tumours when compared with the same total dose given in longer treatment time as in more conventional fractionation schedules.

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Design of a database with graphical analysis for X-ray quality assurance and dose information to assist in a programme for patient dose reduction

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Abstract. A database system has been set up on an IBM PC to store X-ray quality assurance (QA) data and patient doses for all X-ray equipment operated by Grampian Health Board. Graphical analysis facilities have been developed to display data in a readily understandable form. Data on equipment specifications, QA test results, exposure factors for standard examinations, and thermoluminescent dosimeter (TLD) measurements of patient skin doses are stored in separate forms. X-ray machine outputs are fitted to a simple polynomial equation, and the data combined with information on exposure factors to calculate entrance doses for selected examinations. Data such as filtration and backscatter factors are derived from look-up tables for use in dose calculations. Histogram comparisons can be made between calculated doses, means of TLD measurements and National Radiological Protection Board reference levels to allow units giving high skin doses to be identified so that corrective action can be taken.

Medical irradiation comprises 87% of the radiation dose to the population from man-made sources in the United Kingdom (Hughes et al, 1989). There are large variations in exposure between similar radiological examinations in different hospitals (Harrison et al, 1983; Shrimpton et al, 1986). An increasing emphasis is, therefore, being placed on maintaining the quality of performance of X-ray equipment and keeping doses to patients to a minimum (National Radiological Protection Board (NRPB), 1990). Regular quality assurance (QA) tests on X-ray equipment can identify faults and provide an early warning of gradual deteriorations in performance, which might otherwise go unnoticed. In addition, if doses to patients are to be reduced, there is a need to make radiologists and radiographers aware of their performance through the regular provision of dose information and how this relates to generally accepted practice.

Data on machine outputs can be employed to estimate patient entrance skin doses. These doses can be used, with thermoluminescent dosimeter (TLD) measurements, to identify units where doses to patients are larger. However, manual calculations and comparisons of the amounts of data involved, and presentation of results in a readily understandable form, are all time consuming. The use of a computerized database system allows efficient data storage and retrieval of QA information. Sophisticated software packages for developing relational databases and producing high-

quality graphics in personal computer systems are now available.

A database has been set up to store results from QA tests, data on exposure parameters and TLD dose measurements for all X-ray units operated by Grampian Health Board. Software routines have been written to calculate mean entrance doses from machine output data or TLD measurements, and display the information in a form that enables continual assessments of equipment performance and patient doses to be made.

Design of the database

In relational database software packages, such as DataEase, dBASE IV, and R:base 5000, data are integrated into a set of related files which can be shared between different applications. The data are accessed through a Database Management System, which simplifies the design of a user interface. DataEase was used for the implementation of the database (DataEase, 1988). It provides a custom menu design and can be linked with Graftalk, a package that facilitates graphical analysis of database information (DataEase, 1987).

The database was designed with five primary forms (Fig. 1), which are the key forms used in record entry. The form "Equipment" stores information on each unit, such as manufacturer, model and serial numbers, and dates of manufacture and installation as required by the *Ionising Radiation Regulations* (IRR, 1988). There is one entry for each unit operated by the Health Board, and each is given a unique identity code. The first two letters represent the name of the hospital department, the next two digits the number of the unit, and the last two letters the type of equipment. Associated tables are used

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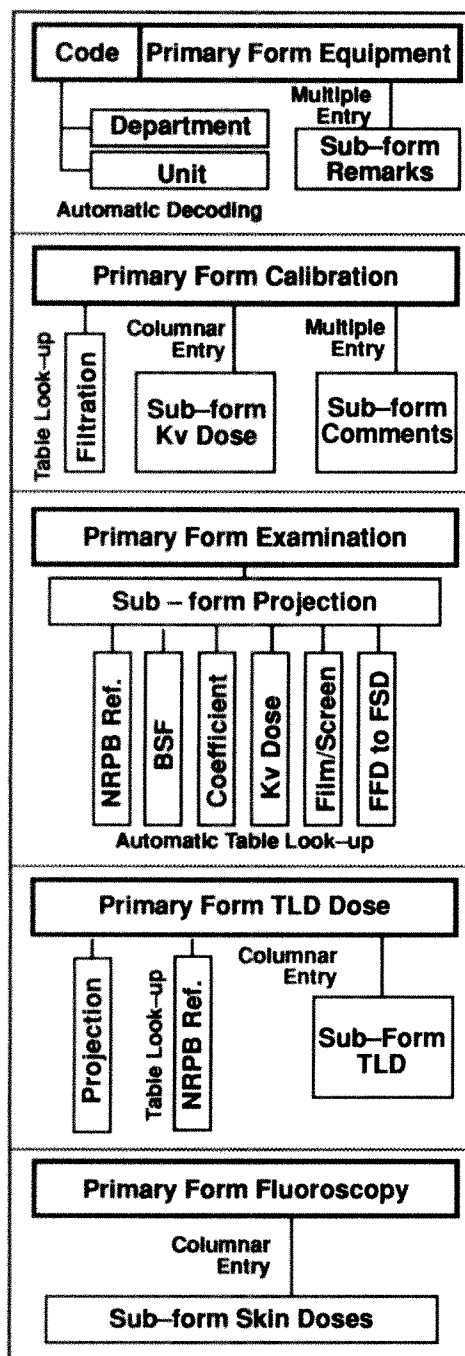


Figure 1. Primary forms used for data storage, with associated sub-forms and tables.

to decipher the code to speed up data entry. The other four primary forms contain results of measurements or exposure factors and each record is uniquely identified by the equipment code and the date of the test. "Calibration" contains results of QA tests, "Examination" has exposure factors for standard examinations,

"TLD Dose" contains results of TLD measurements for single radiographs, and "Fluoroscopy" has information on doses received during fluoroscopic examinations.

Numerous sub-forms have been constructed (Fig. 1). Some are used to facilitate data entry in columnar form, and others provide the flexibility to write short or long entries by allowing several fields to be linked together. These are useful for storing remarks about particular units. Tables have been designed to provide automatic entry for information linked to key fields, and to provide reference data for calculations.

Data entry, viewing and analysis is carried out through several tiers of menus, the first tier of which is shown in Fig. 2. The programs written occupy less than 0.4 Mbytes of memory and the data stored so far for Grampian Health Board Units about 0.9 Mbytes. All data for tests carried out on the 70 fixed units, 50 mobiles and 70 dental units in Grampian, over a 1 year period, can be stored on one 2 Mbyte floppy disk.

Quality assurance data

Protocols similar to those described in the literature were used for the QA tests (Hospital Physicists' Association (HPA), 1980). Results entered into the database include errors in kV and exposure time, percentage variations in output at particular settings, and information on alignment of the light beam and X-ray fields. The aluminium half-value thickness at 80 kV, or a specified alternative kV is also entered, and the filtration automatically evaluated from a look-up table. Data on outputs at different kV and mA settings are recorded in columnar form in sub-form "Kv Dose" (Fig. 1). The outputs are automatically corrected to a standard distance 0.75 m and 20 mAs. A second sub-form "Comments" is used to store more information on equipment performance and details of any corrective action required. Data in the form can be printed as a QA report. The relationship between output and mA setting is assessed by plotting a linear regression fit using the option offered by Graftalk (DataEase, 1987). The variation in output with kV settings is plotted with a curve depicting a quadratic relationship with a coefficient equal to the mean value for $\text{Output}/(\text{kV})^2$ derived from all the data. The fit is improved by entering alternative coefficients of the equation ($\text{Output} = a[\text{kV}]^2 + b[\text{kV}] + c$). The coefficients selected are then stored in a table "Coefficient" for use in calculating outputs for different kV settings (Fig. 1).

Entrance dose calculations

The primary form "Examination" is used to store information on exposure factors and filament-to-skin distance (FSD) for standard radiographic examinations with each unit. Those chosen were the simple examinations included in the NRPB survey (Shrimpton et al, 1986), namely lumbar spine, chest, skull, abdomen, thoracic spine and pelvis, and also the knee used in a previous study in Grampian. Radiation Protection Supervisors in each department were asked to complete forms from which mean factors were derived for every

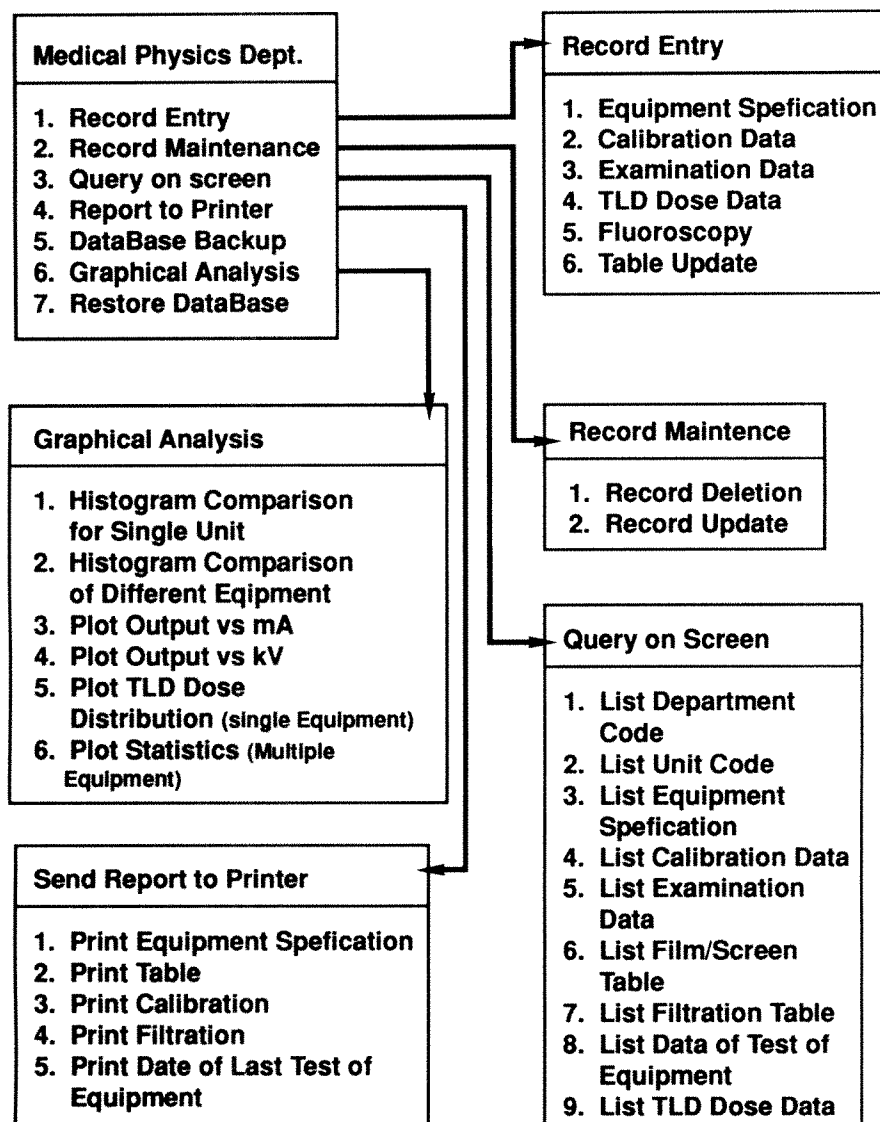


Figure 2. First tier of database menus. Option 1 provides data entry into the five primary forms, options 3 and 4 provide information on screen or as a printout, and option 6 provides histogram analysis of dose information and plots of output data.

projection for each type of examination. Results for fixed units, on which particular examinations were carried out regularly, were derived from groups of patients examined, while data for other examinations and for mobile units took the form of accepted average exposure factors used. In a few cases, filament-to-film distance (FFD) was given instead of FSD, so a table was compiled from measurements on several units, to allow conversion from FFD to FSD for each projection, so that approximate calculations could be carried out before actual measured distances were available. Information on the film/screen combination and film size was also included for reference. The primary form is linked with a sub-form

“Projection” to enable data entry for different projections for one examination in columnar mode (Fig. 1). Since X-ray output measurements had been stored in the form “Calibration” for a range of kV at 20 mAs and 0.75 m, skin entrance doses (D_{skin}) could be calculated automatically from the equation:

$$D_{\text{skin}} = D_{\text{air}} \frac{(\mu/\rho)_{\text{muscle}}}{(\mu/\rho)_{\text{air}}} \times \frac{\text{mAs}}{20} \times \left(\frac{0.75}{\text{FSD}} \right)^2 \times \text{BSF}$$

where (μ/ρ) are the ratios of mass absorption coefficients to densities. The ratio of these quantities for muscle and air can be taken as 1.06 for all typical diagnostic X-ray

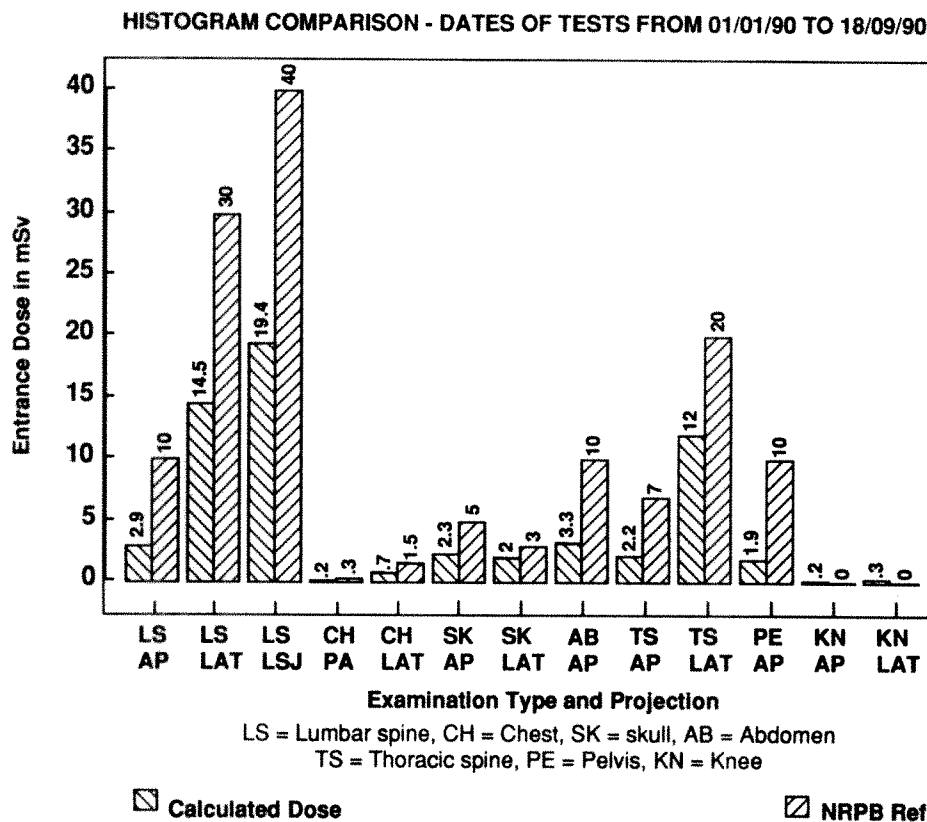


Figure 3. Display option showing histogram comparison of patient entrance doses and NRPB reference levels for selected examinations and projections, for one piece of equipment.

qualities (Wall et al, 1988); BSF is the backscatter factor. A value of dose output in air (D_{air}) in mGy is supplied to the sub-form "Projection" when the fields "Code" and "kVp" in the forms "Examination" and "Calibration" are matched. If no output measurement has been made at the kV used, a dose will be calculated from coefficients derived from a fit of the output data and stored in the table "Coefficient".

The BSF values are derived from a table "BSF factor" containing data calculated by Monte Carlo techniques (Jones & Wall, 1985). It will supply the appropriate BSF when fields indicating the "Type of Examination", "Projection" and "kVp" are matched. Data corresponding to tube potentials from 50 to 140 kV in steps of 10 kV are stored in the table. The appropriate BSF value for the nearest kV is selected from the table without interpolation. In the first version of the database, a table of BSFs was constructed for a filtration of 3 mm aluminium equivalent. A table of offset values for 2.5 mm and 4 mm was later compiled, which modified the value of BSF when the filtration was less than 2.8 mm, or over 3.5 mm. The table has not been expanded to include offset values for intermediate filtrations, as the addition of 1 mm only changes the result by 1 or 2%.

TLD dose measurements

The fourth primary form "TLD Dose" contains TLD measurements of entrance doses for the radiographic examinations listed in the previous section. The exposure factors and FSD are entered, to allow the TLD result to be compared with the calculated entrance dose. A table "NRPB References" contains reference entrance doses for all combinations of radiographic examination types and projections recommended by the NRPB (Shrimpton et al, 1989). These results are derived from the third-quartile values for the distribution of mean doses at hospitals included in the national survey, and can be used as a baseline for comparison of doses from different units. When the fields "Type of Examination" and "Projection" are matched, the corresponding reference dose is transferred to a virtual field in the sub-form "Projection" for display, as data are entered.

The fifth primary form "Fluoroscopy" contains data and TLD measurements for complex examinations involving both fluoroscopy and radiography. TLD dosimeters are worn throughout the examination, and fields are provided for five selected locations—thyroid, left and right breast, and left and right back—similar to those employed in the NRPB survey (Shrimpton et al, 1986) or other fields as required. Fields are also

provided for the screening time, kV, the number of radiographs taken, the dose-area product for the examination, for units where a dose-area product meter has been installed, and the initials of the radiologist carrying out the examination.

Data analysis

All information retrieval in the database is done by DataEase Query Language processing procedures (DataEase, 1988) and reports are sent to the screen, disk or printer in predetermined formats provided by DataEase. The frequency distribution of TLD measurements of one type of examination and projection for one or a group of units can be displayed as a histogram. Dates defining the period over which results are required are entered, so that the impact of changes in equipment and techniques can be monitored.

For any single unit the calculated skin doses or the mean of TLD measurements for each projection of different types of examinations can be compared with the NRPB reference levels, or other selected standard, by means of bar charts (Fig. 3). This enables the user to pin-point doses that are higher than a reference level, so that an investigation into the causes can be carried out and corrective action taken. Again the dates defining the period for which results are required can be selected, and calculated doses can be compared with mean results from TLD measurements in order to assess their accuracy. Measurements for one type of examination for several pieces of equipment can be compared to monitor the performance of mobile or other units used for a limited range of examinations. Fluoroscopic data are, at present, simply viewed through histogram comparisons of doses at different locations.

Conclusions

Software packages, costing a few hundred pounds, have been used to develop a database for handling and analysing data from a QA programme. The ability for rapid retrieval of information, coupled with the use of graphical display facilities, allows the assessment of QA and patient dose data to be carried out rapidly and efficiently. The use of mean exposure factors, contained in the form "Examination", allows a simple assessment of the level of entrance skin doses for a particular unit to be made. Units where the values are above or similar

to the NRPB reference levels can then be targeted for more detailed study with TLD measurements, and reasons for the higher doses sought, so that appropriate corrective action can be taken. The database will allow changes in equipment performance to be monitored more closely, and provide data in a readily accessible form for use in estimating doses to patients, when required.

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Memorandum from the Institute of Physical Sciences in Medicine

Back-scatter and F-factors for low- and medium-energy X-ray beams in radiotherapy

Summary of recommendations by a working party of the Institute of Physical Sciences in Medicine

This memorandum has been authorized by the Scientific Committee of the IPSM. The members of the working party were: S. C. Klevenhagen (chairman), R. J. Aukett, J. E. Burns, R. M. Harrison, R. T. Knight, A. E. Nahum and K. E. Rosser. Thanks are due to J. E. Burns for preparing the several drafts on which this summary and the full report are based. The full report of the working party is published in *Physics in Medicine and Biology* (IPSM, 1991).

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Keywords: Dosimetry for radiotherapy, Back-scatter, Low-energy X-radiation

At present, the dosimetry of low- and medium-energy X-radiation for radiotherapy purposes in the UK is based on the method recommended in International Commission on Radiation Units and Measurements (ICRU) Report 23 (1973), and incorporated into the current Hospital Physicists' Association (HPA) code of practice (1983). The essential points are summarized here using the same symbols and units as in the code of practice.

For an X-ray beam between 150 kV and 300 kV (0.5 mm Cu and 4 mm Cu half-value layer (HVL)), ICRU recommended that output measurements should be made using an ionization chamber with its centre 5 cm deep in a water phantom. Absorbed dose is given by:

$$D = 1.145 R N_k F \quad (1a)$$

or by:

$$D = 0.01 R N_x F \quad (1b)$$

where D = absorbed dose to water in grays at the position of the centre of the chamber, with the chamber replaced by water, R = instrument reading, corrected to the same standard ambient conditions as the calibration factor, N_k = calibration factor to convert the instrument reading to air kerma in grays for standard ambient conditions (at present 20°C, 1013 mbar, and 50% RH for calibrations at NPL), N_x = calibration factor to convert the instrument reading to exposure in röntgens for standard ambient conditions, F = a conversion factor, in rad/röntgen, which depends on the HVL of the X-ray beam being used.

For an X-ray beam between 40 kV and 150 kV (0.5 mm Al and 8 mm Al HVL), ICRU recommended that output measurements should be made with the chamber under scatter-free conditions in air on the

beam axis, at a distance from the target equal to the source-surface distance (SSD) normally used. The absorbed dose to water in grays on the beam axis at the surface of a water phantom is given by:

$$D = 1.145 R N_k FB \quad (2a)$$

or by:

$$D = 0.01 R N_x FB \quad (2b)$$

where the symbols have the same meanings as in equations 1a and 1b, with the addition that B is the back-scatter factor appropriate to the field size and radiation quality used.

The HPA code of practice recommended that values of back-scatter factors should be derived from BJR Supplement 17 (1983), and F-factors from ICRU Report 23 (1973). However, in 1987 the International Atomic Energy Agency (IAEA) published a code of practice with different values of back-scatter factors and procedures for converting air kerma into absorbed dose to water that give different results from those obtained using the HPA code of practice.

The Institute of Physical Sciences in Medicine (IPSM) therefore set up a working party to examine the two discrepancies and to recommend what action should be taken. This paper contains a summary of its recommendations; a fuller account is published elsewhere (IPSM, 1991).

Back-scatter factors

IAEA back-scatter data

In 1984 Grosswendt used Monte Carlo methods to calculate back-scatter factors for X-radiation generated at voltages between 10 kV and 100 kV, and at 100 cm SSD. His data were subsequently used in the IAEA code of practice (IAEA, 1987) and recommended for use in radiotherapy. These new values differed considerably from those in BJR Supplement 17 (1983), particularly for HVLs between 0.1 mm Al and 1.0 mm Al.

Reprints can be obtained from The British Institute of Radiology, 36 Portland Place, London W1N 4AT, at a cost of £2.00 plus postage.

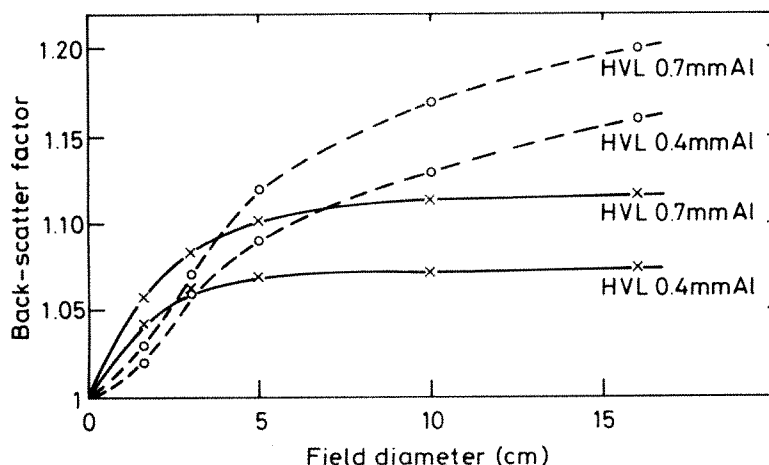


Figure 1. Circles and dashed lines are back-scatter factors in BJR Supplement 17. Crosses and continuous lines are new back-scatter factors in this report.

In a later paper, Grosswendt (1990) extended the X-ray energy range upwards to 280 kV generating potential, and included 661 keV Cs-137 gamma-radiation; back-scatter factors were calculated for a range of SSDs from 10 cm to 100 cm, and for field sizes from 1 cm to 20 cm diameter.

Results from working party

In order to discover which set of values was correct, the IPSM working party re-determined back-scatter factors both by calculation and experiment, paying particular attention to energies below 1 mm Al HVL, where the discrepancies appeared to be greatest.

Knight and Nahum (1990) used Monte Carlo methods to calculate back-scatter factors; their values agree to about 1% with Grosswendt (1990) and also with the back-scatter factors in BJR Supplement 17 (1983) for medium-energy X-radiation above 0.5 mm Cu HVL. Back-scatter factors measured using a flat ionization chamber (Klevenhagen, 1989) are in excellent agreement with Grosswendt except for small fields (5 cm diameter and smaller) at 4 mm Al HVL where they are about 3% lower. Measurements using thermoluminescent dosimeters (Harrison et al, 1990) show the rather larger random scatter which is expected when using this type of dosimeter, but they agree much better with Grosswendt (1990) than with BJR Supplement 17.

Effect of source-surface distance and phantom thickness

Grosswendt's (1990) calculations in the range 10–100 cm SSD showed that back-scatter factors increase with increasing SSD, particularly for large fields and for X-radiation above 1.0 mm Al HVL; this has been confirmed by Knight and Nahum (1990). The new values presented in this report take this effect into account.

All the calculations and measurements discussed so far are for a thick phantom, giving nearly full back-scatter. Quimby et al (1938) and Wachsmann et al (1954) showed that back-scatter decreases as the

phantom thickness is decreased. Klevenhagen (1982) provided formulae for calculating the magnitude of this effect and discussed the effect of SSD on the build-up of back-scatter with phantom thickness.

Effect of X-ray spectrum

The effect on the back-scatter factor of different X-ray spectra for a given HVL appears to be rather uncertain, with conflicting evidence given by Johns et al (1954) and Harrison (1982).

Burns (1975) surveyed the radiological literature on the range of kV-filter combinations used in radiotherapy and found that when kV was plotted against HVL on log-log graph paper, the results clustered around a straight line. The qualities used by Grosswendt (1990) for his Monte Carlo calculations of back-scatter also lie on or close to the same straight line. Therefore, it was assumed that the qualities he used are typical of those found in radiotherapy, and the working party decided to use his values as the basis for new back-scatter factors to replace those in BJR Supplement 17.

Handling of the data for this report

Grosswendt's back-scatter factors were plotted against HVL in order to interpolate values for the HVLs found in BJR Supplement 17. Some smoothing was necessary and the data of Knight and Nahum (1990) and Klevenhagen (1989) were used to confirm the appropriate shape of the curves. The data were also plotted against field size and SSD in order to interpolate back-scatter factors for the field sizes and SSDs published in BJR Supplement 17, and were then rounded to 1%.

The final values are presented in Tables 1.3 and 1.4 in a form that matches the irradiation conditions and format used in BJR Supplement 17. Table numbers are the same as the corresponding tables in that publication.

Comparison of new and old back-scatter factors

The greatest change in back-scatter occurs between 0.1 mm Al and 1.0 mm Al HVL for large field sizes. The

Tables 1.3

Corrected values of back-scatter factors for Tables 1.3 in *Central Axis Depth Dose Data for Use in Radiotherapy*, BJR Supplement 17 (1983)

Table 1.3.1. HVL 0.01 mm Al

SSD (cm)	10
Diameter (cm)	1.6–5.0
BSF	1.00

Table 1.3.2. HVL 0.02 mm Al

SSD (cm)	10
Diameter (cm)	1.6–5.0
BSF	1.00

Table 1.3.3. HVL 0.04 mm Al

SSD (cm)	10	20	30
Diameter (cm)	1.6–5.0	1.6–10.0	3.0–16.0
BSF	1.01	1.01	1.01

Table 1.3.4. HVL 0.07 mm Al

SSD (cm)	10	20	30
Diameter (cm)	1.6–5.0	1.6–10.0	3.0–16.0
BSF	1.01	1.01	1.01

Table 1.3.5. HVL 0.10 mm Al

SSD (cm)	10	20	30
Diameter (cm)	1.6–5.0	1.6–10.0	3.0–16.0
BSF	1.02	1.02	1.02

Table 1.3.6. HVL 0.20 mm Al

SSD (cm)	10	20	30
Diameter (cm)	1.6–5.0	1.6–10.0	3.0–16.0
BSF	1.03–1.04	1.03–1.04	1.03–1.04

Table 1.3.7. HVL 0.40 mm Al

SSD (cm)	10			15			30			
Diameter (cm)	1.6	3.0	5.0	1.6	3.0	5.0	3.0	5.0	10.0	16.0
BSF	1.04	1.06	1.07	1.04	1.06	1.07	1.06	1.07	1.07	1.07

Table 1.3.8. HVL 0.70 mm Al

SSD (cm)	10			15			30			
Diameter (cm)	1.6	3.0	5.0	1.6	3.0	5.0	3.0	5.0	10.0	16.0
BSF	1.06	1.08	1.10	1.06	1.09	1.10	1.09	1.10	1.12	1.12

Tables 1.4

Corrected values of back-scatter factors for Tables 1.4 in *Central Axis Depth Dose Data for Use in Radiotherapy*, BJR Supplement 17 (1983)

Table 1.4.1. HVL 1.0 mm Al

Diameter (cm)	0	1	2	3	4	5	6	8	10	15	20
SSD											
10 cm	1.0	1.05	1.09	1.10	1.12	1.12	1.13	1.14	1.15		
15 cm	1.0	1.05	1.09	1.10	1.12	1.13	1.14	1.15	1.16		
20 cm	1.0	1.05	1.09	1.10	1.12	1.13	1.14	1.15	1.16	1.16	
25 cm	1.0	1.05	1.09	1.10	1.12	1.13	1.14	1.15	1.16	1.17	1.17
30 cm	1.0	1.05	1.09	1.10	1.12	1.13	1.14	1.15	1.16	1.17	1.17

Table 1.4.2. HVL 2.0 mm Al

Diameter (cm)	0	1	2	3	4	5	6	8	10	15	20
SSD											
10 cm	1.0	1.06	1.11	1.14	1.16	1.17	1.18	1.20	1.22		
15 cm	1.0	1.06	1.11	1.14	1.16	1.18	1.19	1.21	1.23		
20 cm	1.0	1.06	1.11	1.14	1.16	1.18	1.19	1.22	1.23	1.26	
25 cm	1.0	1.06	1.11	1.14	1.16	1.18	1.20	1.22	1.24	1.26	1.27
30 cm	1.0	1.06	1.11	1.14	1.16	1.18	1.20	1.22	1.24	1.27	1.28

Table 1.4.3. HVL 3.0 mm Al

Diameter (cm)	0	1	2	3	4	5	6	8	10	15	20
SSD											
10 cm	1.0	1.06	1.12	1.16	1.18	1.20	1.22	1.25	1.26		
15 cm	1.0	1.06	1.12	1.16	1.18	1.21	1.23	1.25	1.27		
20 cm	1.0	1.06	1.12	1.16	1.19	1.21	1.23	1.26	1.28	1.32	
25 cm	1.0	1.06	1.12	1.16	1.19	1.21	1.24	1.26	1.29	1.32	1.34
30 cm	1.0	1.06	1.12	1.16	1.19	1.22	1.24	1.27	1.29	1.33	1.35

Table 1.4.4. HVL 4.0 mm Al

Diameter (cm)	0	1	2	3	4	5	6	8	10	15	20
SSD											
10 cm	1.0	1.06	1.12	1.16	1.20	1.22	1.24	1.27	1.29		
15 cm	1.0	1.06	1.12	1.16	1.20	1.22	1.25	1.28	1.31		
20 cm	1.0	1.06	1.12	1.16	1.20	1.23	1.25	1.29	1.32	1.36	
25 cm	1.0	1.06	1.12	1.16	1.20	1.23	1.25	1.30	1.32	1.37	1.39
30 cm	1.0	1.06	1.12	1.17	1.20	1.23	1.26	1.30	1.33	1.38	1.40

Table 1.4.5. HVL 8.0 mm Al

Diameter (cm)	0	1	2	3	4	5	6	8	10	15	20
SSD											
10 cm	1.0	1.05	1.11	1.15	1.19	1.22	1.25	1.29	1.32		
15 cm	1.0	1.05	1.11	1.15	1.19	1.23	1.26	1.30	1.34		
20 cm	1.0	1.05	1.11	1.15	1.20	1.23	1.26	1.31	1.35	1.41	
25 cm	1.0	1.05	1.11	1.15	1.20	1.24	1.27	1.32	1.36	1.42	1.45
30 cm	1.0	1.05	1.11	1.16	1.20	1.24	1.27	1.32	1.36	1.43	1.46

new back-scatter factors reach their maximum values for much smaller field sizes than those in BJR Supplement 17, as shown in Figure 1. Changes for HVLs between 1.0 mm Al to 8 mm Al are less marked.

No new data are provided for medium-energy X-radiation (0.5 mm Cu to 4 mm Cu HVL), because the values of Grosswendt (1990), supported by Knight and Nahum (1990), agree so well with those in BJR Supplement 17 that corrections are unnecessary.

No data are available to derive back-scatter factors for the two short SSD X-ray units which are dealt with in Tables 1.2 of BJR Supplement 17.

Earlier published back-scatter factors

When comparing the results of radiotherapy over a number of years, it is desirable to correct for any changes to the back-scatter factors that have been used to calculate the exposure or dose received by patients. In the UK, back-scatter factors have generally been taken from data published in the British Journal of Radiology.

The first review of back-scatter factors was published by Mayneord and Lamerton (1941) and covered the medium- and high-energy X-ray range from 0.5 mm Cu to 17 mm Cu HVL. The first supplement of the British Journal of Radiology to publish back-scatter data was Supplement 5 (1953); this covered the low-energy range (0.01–8 mm Al HVL) only.

In the next relevant BJR supplement to be published (BJR Supplement 10, 1961), back-scatter factors for low-energy X-radiation were significantly different from those in BJR Supplement 5 (1953), and the back-scatter factors for medium-energy X-radiation differed significantly from those published by Mayneord and Lamerton (1941). However, back-scatter factors then remained unchanged through BJR Supplement 11 (1972) to the most recent BJR Supplement 17 (1983), except for a slight change in the values for 4 mm Cu HVL in Supplement 17. The new back-scatter factors in this report therefore represent the first change in recommended values for radiotherapy since BJR Supplement 10 in 1961.

Recommendation on back-scatter factors by working party

The IPSM working party recommends that, for radiotherapy dosimetry, the new back-scatter factors in Tables 1.3 and 1.4 should be used in place of those in the corresponding tables of BJR Supplement 17. It suggests that no change should be made in the back-scatter factors for short SSDs given in Tables 1.2 of BJR Supplement 17 until more accurate data become available.

Dose-conversion F-factors

In 1987 the IAEA published a code of practice which recommended procedures for converting the response of an ionization chamber calibrated in terms of air kerma into absorbed dose to water for medium-energy X-radiation. These give rise to different results from those obtained using the current HPA code of practice (HPA, 1983).

Table 2. Values of the conversion factor F , taken from ICRU Report 23

HVL of primary beam	F (rad/R)
(mm Al)	
0.5	0.89
1.0	0.88
2.0	0.87
4.0	0.87
6.0	0.88
8.0	0.89
(mm Cu)	
0.5	0.89
1.0	0.91
1.5	0.93
2.0	0.94
3.0	0.95
4.0	0.96

If absorbed dose to water is calculated from a measurement with a chamber in air, together with the application of a back-scatter factor, the difference between the two codes of practice is not large, amounting to 2% at about 0.1 mm Cu HVL and decreasing for larger HVLs until the results almost agree at about 4 mm Cu HVL.

However, for X-ray beams with generating potentials of 100 kV and above (about 0.2 mm Cu HVL), the IAEA code of practice recommends that measurements should be carried out with the chamber inserted into a water phantom and claims that a correction must be applied for the effect of displacing water by the chamber. The use of the IAEA code gives values of absorbed dose that are 12% higher than those obtained using the HPA code of practice at 100 kV. This discrepancy decreases for higher HVLs, becoming only about 1% at 4 mm Cu HVL.

The IPSM working party compared the HPA and IAEA codes of practice with results reported in four scientific papers. Two of these papers compared absorbed dose, determined using the method described in the HPA code of practice, with absorbed dose derived from calorimetric measurements. The other two papers reported determinations of the effect of displacing phantom material by an ionization chamber. The papers are not in exact agreement with each other, but they do tend to support results obtained using the HPA code of practice rather than the IAEA code.

In view of this evidence the IPSM working party recommends that no change should be made to the procedure for converting air kerma (or exposure) into absorbed dose to water for medium-energy X-radiation for the time being, until more work on this subject is published. A more detailed justification for this recommendation is contained in the report of the working party (IPSM, 1991). The HPA and IAEA conversion procedures are also compared and discussed by Rosser (1991).

For convenience, the values of the dose-conversion F-factors in the current HPA code of practice are reproduced here as Table 2, to be used in Equations 1 or 2 as appropriate.

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Technical note

Measuring the filtration of mammographic X-ray tubes with molybdenum targets

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The method employed in this work, to estimate the filtration of mammographic X-ray sets, makes use of the measurement of the half-value layer (HVL) of the X-ray beam, which is filtered by the air path, the X-ray tube window, an added molybdenum filter and a known thickness of Perspex. Sets of data have been calculated that relate the measured HVL to the added molybdenum filter thickness. The mammographic X-ray sets included in this study were all Siemens Mammomat 2 type, which have molybdenum targets and molybdenum filters and the compression plates employed have a Perspex equivalence of about 1 mm or 2 mm. The kilovoltage is produced by a high-frequency generator and has a nominally constant potential waveform.

It is often necessary to determine the HVL of mammographic X-ray sets, for two different reasons: (a) measurement of mean glandular breast dose (Institute of Physical Sciences in Medicine (IPSM), 1989), and (b) determination of total filtration by the HVL method. The estimation of total filtration of X-ray tubes with tungsten targets has previously been given some attention by the author (Cranley & Fogarty, 1988). In addition, errors in the HVL method have been analysed (Gilmore & Cranley, 1990).

The IPSM method of estimating breast dose has become widely adopted by physicists involved in the NHS Breast Screening Programme. The method involves the determination of both incident air kerma (for correct exposure of a phantom representing the standard breast) and HVL of the incident X-ray beam. The compression device should be in position for these measurements, to satisfy the standard breast conditions.

It is necessary, therefore, to have the compression device in position during the measurement of the HVL.

The requirement to estimate the filtration of the mammographic X-ray beam comes from the International Commission on Radiation Protection (ICRP) (1982), which recommends that the total permanent filtration should be equivalent to at least 0.5 mm aluminium or 0.03 mm molybdenum. This implies that the total filtration should be estimated with removable filters, such as the compression plate, excluded.

The current method allows the HVL to be measured with the compression plate in position, giving an estimate of the amount of added filtration in microns of molybdenum, or the total filtration (including the compression device) in millimetres of aluminium.

Materials and methods

The known filtration in the X-ray beams examined was 1 mm beryllium in the X-ray tube window, the air path and the compression plate, in addition to the added thickness of molybdenum, and filtration in the anode itself. The anode filtration is already accounted for in the calculation of spectra produced by molybdenum targets at different kilovoltages and at an effective target angle of 15°, and these spectra were attenuated by the known thicknesses of material of the X-ray tube window, air path and compression plate. These spectra were subjected to successive increasing thicknesses of molybdenum attenuation, and the HVL in aluminium equivalence was calculated at each thickness. This allowed the data in Figs 1 and 2 to be produced, for thicknesses of 1 and 2 mm of Perspex compression plate. The data in Fig. 3 were produced by adding increasing thicknesses of aluminium to an X-ray beam with no filtration other than that within the anode.

The data produced in this manner allow an estimate of the thickness of the added molybdenum filter (Figs 1 and 2) and an estimate of aluminium equivalence of the total filtration of the X-ray beam incident on a compressed breast (Fig. 3).

The spectral calculations were performed using the method of Birch and Marshall (1979), and attenuation coefficients were calculated using the data of McMaster et al (1969). No adjustment was made to the constant potential data to account for kilovoltage waveform since none of the X-ray sets examined exhibited kilovoltage ripples in excess of 1 kV, as measured by a Keithley model 35080 kVp divider. The curves in Figs 1-3, derived from mathematically determined spectra, could not be checked in any experimental way other than by comparison of results with measured tube outputs, as in Figs 4 and 5.

SIA grade aluminium foils were used, with nominal thicknesses of 0.1 and 0.2 mm Al, as supplied by Gammex-RMI Ltd. The thicknesses were checked by measuring the areas of the filters, weighing each one using an accurate microbalance and calculating the mean thickness from the density of aluminium. The estimated mean thicknesses were found to be within 4% of the nominal values, and the optimum combination was determined for each required thickness, so that errors of approximately $\pm 1\%$ were not exceeded. The

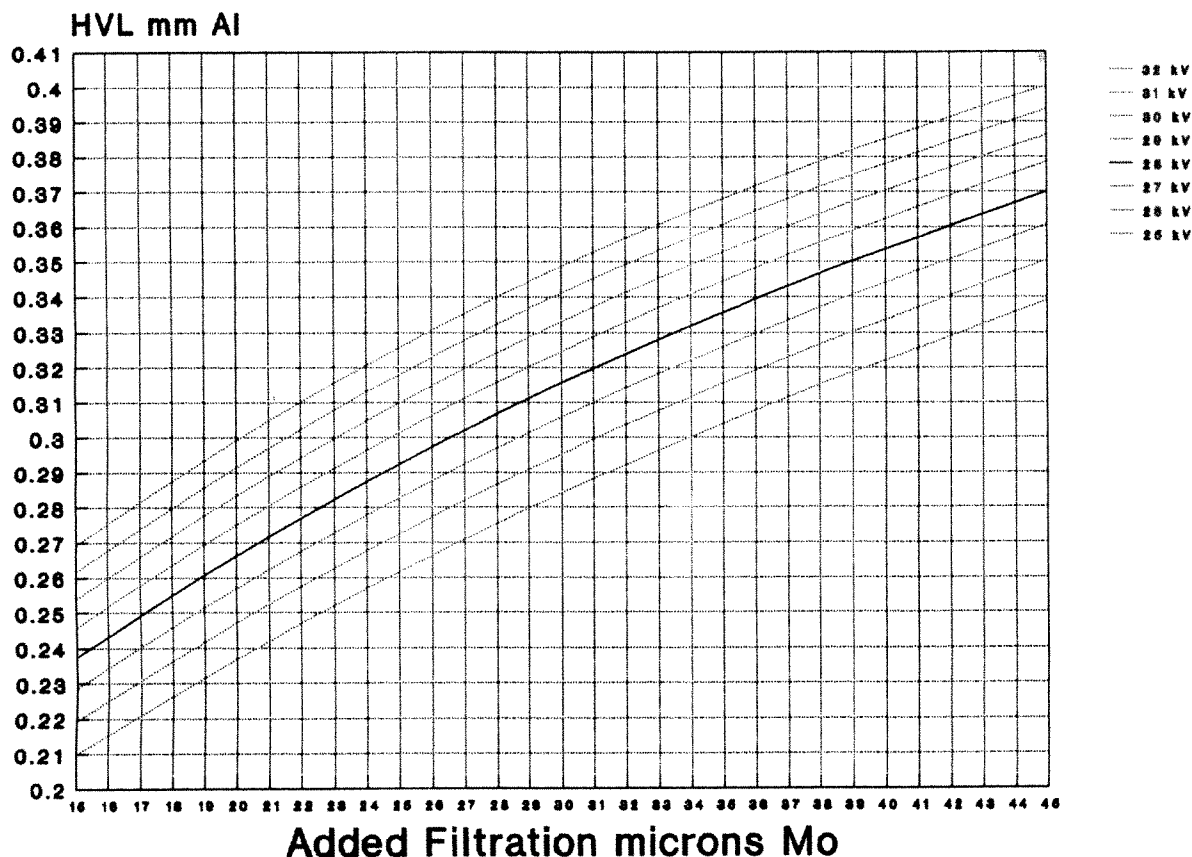


Figure 1. Calculated relationship between HVL and Mo filter thickness for an effective target angle of 15° and constant potential kilovoltage waveform. The assumed filtration is 1 mm Be, 500 mm air and 1 mm Perspex.

filters were marked so that the same combinations were used for all measurements.

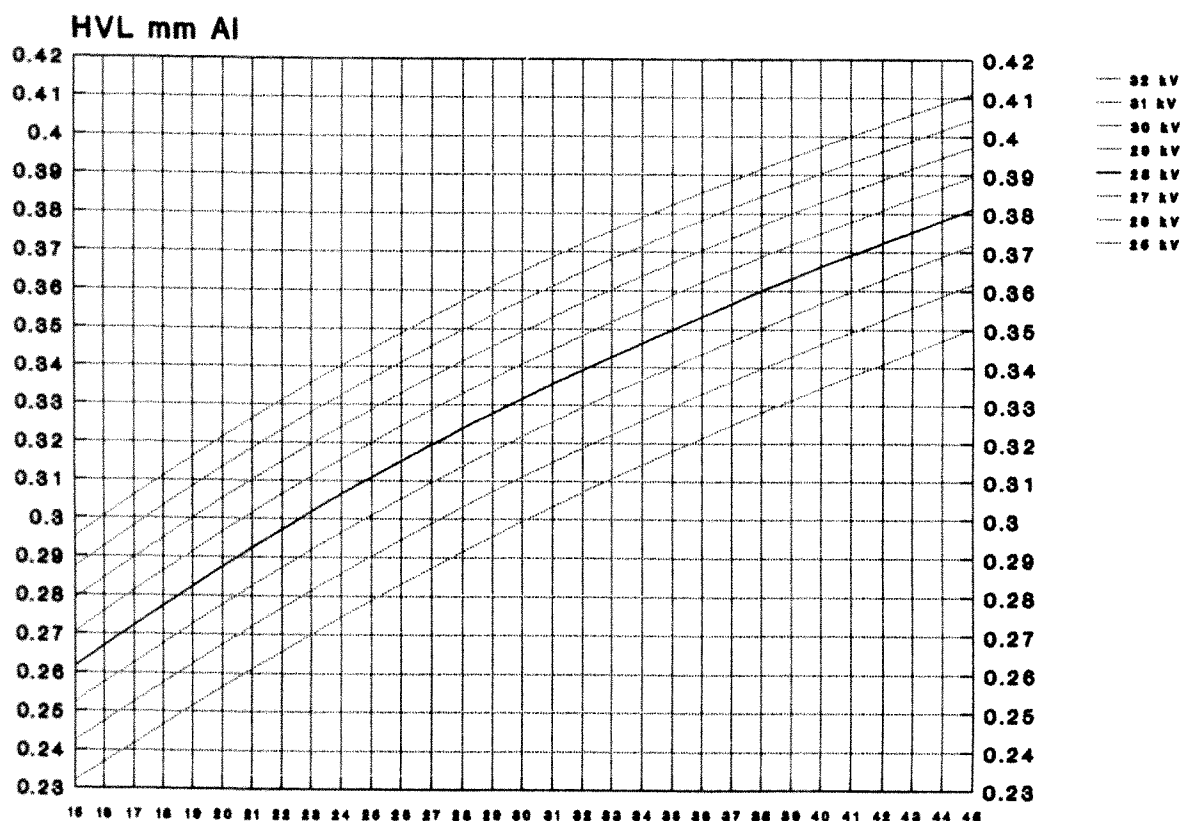
A Radcal Corporation 10X5-6M mammographic ionization chamber was used, which has a solid-back construction and is unaffected by backscatter. This allows the chamber to be placed close to scattering objects such as the breast table itself, without backscatter problems. The chamber was placed at a mean distance of 500 mm from the tube focus and centred on an axis that had been determined to represent radiation emitted from an X-ray tube with a target angle of 15° . This represents the approximate position of the centre of the average-sized breast, rather than the "reference axis", which is usually that from the tube focus to the centre of the film.

The filters are conveniently held in a reproducible position by the compression plate itself, raised to a suitable height to enable positioning as far away from the ionization chamber as possible, reducing the effects of forward scatter but allowing access to the filters. It is important to determine the reproducibility of X-ray tube output by making about eight initial exposure readings. All of the X-ray sets examined here have been shown to have excellent reproducibility (coefficient of variation less than 1%).

Each of the six X-ray sets examined in this study was set to three different kilovoltages, usually 28, 30 and 32 kV, and attenuation curves were determined by increasing the added filtration thickness by 0.1 mm Al and taking exposure measurements until one reading beyond the HVL was achieved. The algorithm used for calculating the HVL from an attenuation curve makes use of one point on either side of the HVL to interpolate the HVL value. It is therefore not necessary to take more than one measurement beyond the HVL. Kilovoltages were measured using a Gammex-RMI model 232 kVp meter, at the same position and mAs value (20 mAs) used for attenuation curves. The kVp meter had recently been compared with 17 other instruments of its type and was shown to be within 0.2 kV of the mean of all these instruments for each of 28, 30 and 32 kV. The manufacturer's specification of accuracy of this meter is $\pm(1 \text{ kV} + 2\%)$.

Experimental results

Figure 4 shows the range of estimated molybdenum filter thicknesses for the six X-ray sets examined. The output values in μGy in air per mAs at 500 mm and 28 kV have been plotted against the estimated



Added Filtration microns Mo

Figure 2. Calculated relationship between HVL and Mo filter thickness for an effective target angle of 15° and constant potential kilovoltage waveform. The assumed filtration is 1 mm Be, 500 mm air and 2 mm Perspex.

molybdenum filter thicknesses since it would be expected that variations in filtration would produce corresponding variations in output. Kilovoltage values

measured had a mean deviation from the nominal value of 0.26 kV and a standard deviation of 0.37 kV.

Figure 5 illustrates the variation in output with estimated total aluminium thickness. Each point represents the mean of estimates made at different kV settings, usually the three values mentioned above.

Figure 6 shows a plot of estimated molybdenum filter thickness against estimated total aluminium equivalence. Again each point represents the mean of estimates made at about three different kilovoltages.

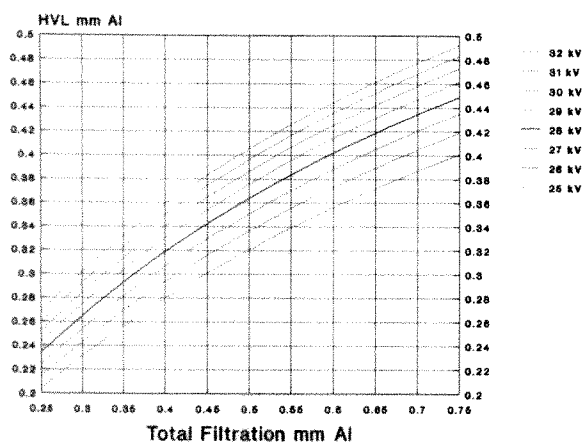


Figure 3. Calculated relationship between HVL and Al filter thickness for an effective target angle of 15° and constant potential kilovoltage waveform.

Discussion

The data presented in Figs 1–3 allow estimates of filtration to be made from measurements of the HVL made for the purposes of estimating mean breast dose to a standard breast phantom. The choice of 1 or 2 mm Perspex allows appropriate data for the compression plate thicknesses to be interpolated.

The accuracy of the method is estimated by the method of Gilmore and Cranley (1990) to be within $\pm 7\%$, and results in Fig. 4 indicate that, within this accuracy, while all the X-ray sets examined have been fitted with molybdenum filters of adequate thickness, the method is sensitive enough to detect small variations

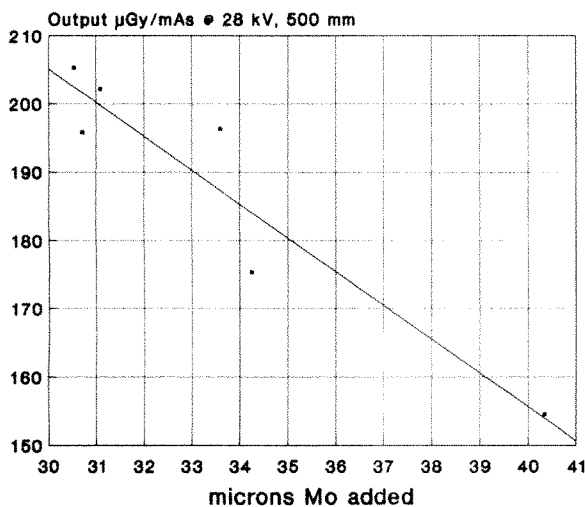


Figure 4. Measured output in μGy in air per mAs at 500 mm against estimated Mo filter thickness for six mammographic X-ray sets. The straight line is a least-squares fit.

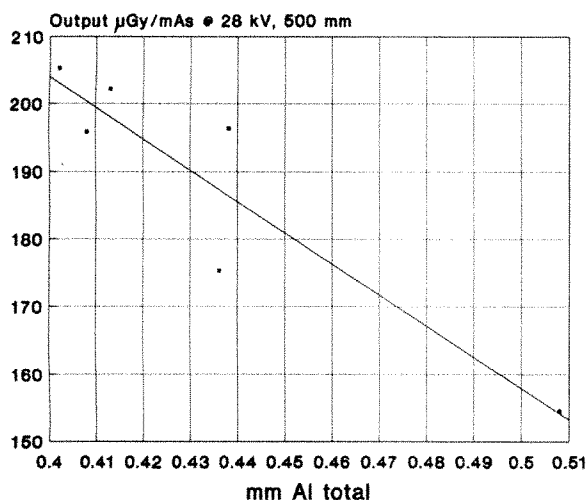


Figure 5. Measured output in μGy in air per mAs at 500 mm against estimated total filtration in Al equivalence for six mammographic X-ray sets. The straight line is a least-squares fit.

in molybdenum filter thickness, reflected in variations in measured output values. Values of molybdenum filtration (Fig. 4) and aluminium filtration (Fig. 5) refer to measured kilovoltage values. The output values reflect fluctuations in the kilovoltage that were not more than ± 1 kV from the nominal 28 kV.

Figure 6 shows the correlation between added molybdenum and total aluminium filtration, estimated from the same sets of experimental data. The fluctuations from the least-squares line fit therefore reflect errors in attenuation coefficients combined with errors introduced by reading filtration values from Figs 1–3. Figure

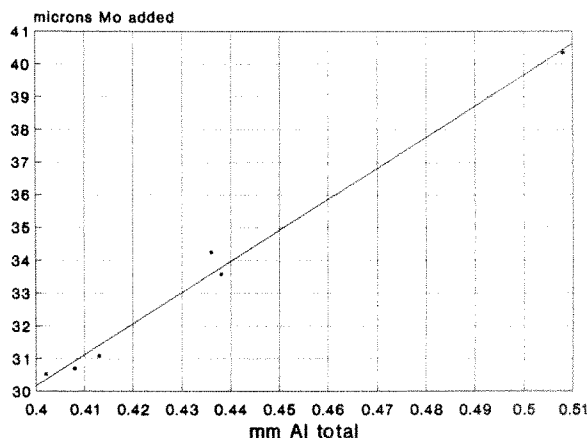


Figure 6. Estimated Mo thickness against estimated total filtration in Al equivalence for six mammographic X-ray sets. The straight line is a least-squares fit.

6 indicates that an aluminium equivalence of 0.5 mm Al does not coincide with the 0.03 mm of molybdenum as suggested by the requirements of the ICRP (1982), and that to achieve this aluminium equivalence, mammography X-ray sets would need to be fitted with considerably more than 0.03 mm molybdenum. However, it is felt that 0.03 mm molybdenum is perfectly adequate for use in mammography.

Acknowledgments

I am grateful to Mr Richard Birch for his helpful communications during this study, and to the radiological departments throughout Northern Ireland where the data were collected. I would like to express appreciation of the work done by Dr A. Underwood and Mr A. Robinson on the intercomparison of kV meters.

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Case reports

Malignant melanoma of the vulva: response to radiation

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Keywords: Melanoma, Vulva, Radiotherapy, Altered fractionation

Although malignant melanoma of the vulva is a relatively rare malignancy with only about 350 cases reported in the literature, in some series it has accounted for a surprising 8-11% of all invasive cancers of the vulva (Morrow, 1981; Jones, 1988). While surgery has remained the treatment of choice, radiation therapy has received very little attention in the management of vulval melanoma. This is despite the fact that clinical responses have been achieved at other sites using high dose fractionation regimens (Habermalz & Fischer, 1976; Strauss et al, 1981). We report a case of melanoma of the vulva where complete clinical regression of both the primary and nodal disease was observed following intermediate dose fractionation, only to be followed by fatal disseminated metastasis 3 months later.

Case report

A 35-year-old woman presented with a history of rapidly increasing pigmented nodules over the vulva with ulceration and discharge. On examination, there was a large mass seen arising from the left labium majus involving the left labium minus, the clitoris, the lower third of the vagina and the recto-vaginal septum. In addition a hard fixed 4 x 3 cm right inguinal node and a mobile 3 x 2 cm left inguinal node were also seen. A biopsy from the lesion was reported as malignant melanoma. The chest X ray done at this time was normal.

The tumour was treated with radical radiotherapy using a cobalt-60 unit with an antero-posterior set up, delivering a dose of 6120 cGy in 17 fractions, using a fractionation schedule of 360 cGy per fraction three times a week (time, dose and fractionation (TDF) factor 128). Initially the treatment included the vulva, both the inguinal fields and the true pelvis to a dose of 3960 cGy, followed by a boost dose of 2160 cGy to the vulva and the inguinal fields only. Near complete regression of the mass was seen following completion of radiotherapy. No enhanced acute reactions were seen during follow-up. 3 weeks following the completion of radiation, complete clinical regression of both the primary and nodal sites were noted.

The patient remained asymptomatic with no evidence of disease till 3 months later when she presented with a nodule in the para-umbilical region. The biopsy of the nodule was reported as consistent with metastatic melanoma. The chest X ray done at this time showed extensive bilateral pulmonary

metastases. The patient died shortly afterwards from progressive respiratory failure.

Discussion

Radical vulvectomy with inguinal dissection has remained the preferred treatment for malignant melanoma of the vulva. Generally considered as a radio-resistant lesion, there have been very few reports of radiotherapy in the primary management of vulval melanoma. Karlen et al (1975) did not note any clinical response in seven patients with melanoma of the vulva. Kolstad (1986) also did not note any response in three patients treated either post-operative or with curative radiotherapy. However, in both these studies the particulars of the radiotherapy were not given.

With conventional fractionation found to be generally ineffective, attention has been focussed on high dose fractionation ranging from 600-900 cGy per fraction for the management of melanoma in general (Overgaard, 1980). Kolstad (1986) advocated the use of 1000 cGy every second day up to 3000 cGy for the management of inoperable recurrent melanoma of the vulva. However, an intermediate dose fractionation was used for the present case to keep the tolerance of the intestines, inguinal and perineal area within acceptable limits.

Patients with deep invasion of the tumour (Clark's level V) in melanoma of the vulva have a 5 year survival of less than 25% (Podrantz, 1983). Similarly lymph nodal metastasis has a 5 year survival of only 14% in vulval melanoma (Morrow & Diasia, 1976). We feel that in the subgroup of patients with extensive loco-regional disease, radical radiotherapy using an intermediate dose fractionation might offer an alternative to surgery as a primary modality of treatment.

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Malignant fibrous histiocytoma: an unusual presentation

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Keywords: Malignant fibrous histiocytoma, Intercranial, Computed tomography

Malignant fibrous histiocytoma (MFH) is the commonest type of adult soft tissue sarcoma (Weiss & Enzinger, 1978). Intracranial MFHs, however, are rare and unreported in children. We report a case of MFH presenting as a posterior fossa mass in a 9-year-old boy with homocystinuria (HCU). This is an unusual presentation and the computed tomography (CT) finding of localized skull vault destruction proved an important differentiating feature from primary posterior fossa tumours. Early diagnosis of MFH is important as primary wide excision of involved bone margins improves prognosis, irrespective of subsequent radiotherapy or adjuvant chemotherapy (Tracy et al, 1984).

Case report

A 9-year-old boy presented with a 4 week history of headaches and vomiting. He had a history of Pyridoxine resistant HCU diagnosed in the neonatal period and had been successfully managed with a low methionine, cystine supplemented diet. On examination there was right sided cerebellar ataxia, sustained nystagmus to rightward gaze but no cranial nerve palsies or papilloedema. The patient's intelligence was normal (IQ was 98), and there was no evidence of lens dislocation or any skeletal manifestations of homocystinuria. The full blood count, erythrocyte sedimentation rate and biochemical profile were normal.

Cranial CT revealed an isodense mass in the right cerebellar region, with contralateral displacement of the fourth ventricle

and dilatation of the third and lateral ventricles. After intravenous contrast the mass demonstrated homogeneous enhancement and was shown to be well defined and bilobular (Fig. 1). The tumour had invaded and destroyed the adjacent occipital bone and there was extension into the superficial soft tissues (Fig. 2).

Surgical exploration revealed a soft tissue mass protruding through the destroyed occipital bone. The posterior fossa

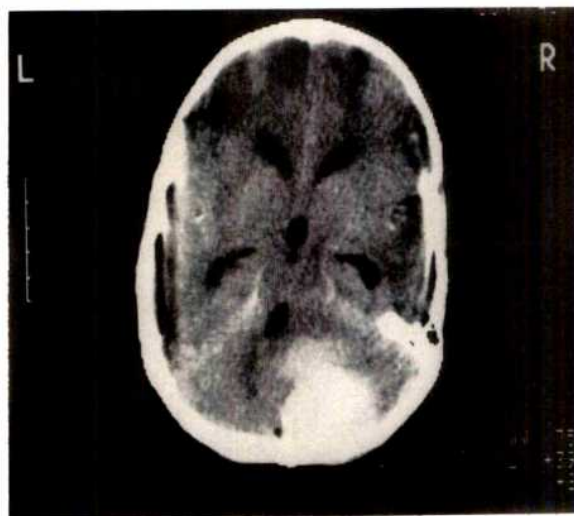


Figure 1. Post-contrast CT scan showing a well defined, bilobular enhancing mass in the right cerebellar region with dilatation of the third and lateral ventricles.

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Figure 2. CT scan at bone settings showing destruction of the right occipital bone and extracranial tumour extension.

tumour was well circumscribed and extended both intradurally and extradurally. The pia mater was intact and no cerebellar involvement could be identified. Microscopic examination showed a tumour composed of a random mixture of histiocytes, fibroblasts and osteoclast type giant cells with areas demonstrating a vague storiform (spoked-wheel) pattern (Fig. 3). The fibroblasts and histiocytes displayed some pleomorphism and mitotic activity. A piece of bone showed infiltration by tumour. A thin fibrous pseudo-capsule was present but in areas this appeared infiltrated by tumour. The tumour was considered to be meningeal in origin. The appearances were those of a giant cell tumour and were classified as a giant cell variant of MFH. CT scans of the thorax, abdomen and pelvis performed after histological diagnosis could identify no metastases or distant primary tumour. Following surgical excision localized cranial irradiation was performed and the patient remains well after 6 months.

Discussion

Primary MFH is one of the commonest adult soft tissue sarcomas occurring most frequently in the seventh decade and involving the extremities in 70% (Weiss & Enzinger, 1978). Primary intracranial MFHs are rare with only 10 reported cases, all in adults and most occurring following cranial radiotherapy for either gliomas or pituitary tumours (Kepes et al, 1973; Gonzales-Vitale et al, 1976; Lam & Colah, 1979; Kalyanaram et al, 1981; Amendola et al, 1985; Sima et al, 1986). Primary intracranial MFHs occur during middle age, are usually supratentorial in site and invariably arise from the meninges. Cerebral metastases from peripheral MFHs are not uncommon (Espana et al, 1980), have a more varied intracranial distribution than primary tumours and are usually found in more elderly patients. This case is unusual because of the patient's age, the tumour site, its homogeneous enhancement and the presence of localized bony infiltration.

Few reviews have considered MFH in children (Cozzutto et al, 1978; Karev, 1979; Tracy et al, 1984),



Figure 3. H&E section showing mixture of histiocytes, fibroblasts and osteoclast type giant cells (object $\times 20$).

reflecting the paucity of tumours (1–2%) in this group. Several differences have been noted in extremity MFHs in children; girls were more commonly affected in contrast to the 2:1 male predominance in adults, and also the prognosis appeared better with a 100% survival at a median of 4 years (Tracy et al, 1984) in one limited study, compared with 60% 2 year survival in most larger adult series. The differential diagnosis of a paediatric posterior fossa mass most commonly includes medulloblastoma, astrocytoma, ependymoma or metastasis. No other lesion was identifiable in this case and the tumour exhibited features atypical of other primary intracranial tumours. With the exception of metastases, skull vault destruction is not a recognized feature in posterior fossa tumours, although bone erosion has been reported in adults with aggressive supratentorial gliomas.

Feldman and Newman (1972) described bony involvement in association with MFH in 25% of cases, of which 75% were thought to represent localized infiltration. The remaining 25% were considered to have arisen primarily from bone. Localized skull base destruction has been documented secondary to a nasopharyngeal MFH (Feldman & Newman, 1972), but never from an intracranial tumour. Calvarial involvement is usually extensive, permeative and unifocal unlike other more common pathologies, such as myeloma and metastases which appear as multifocal well defined lytic foci (Feldman & Newman, 1972).

There have been few descriptions of the CT appearances of intracranial MFH (Sima et al, 1986; Simpson et al, 1986; Schrader et al, 1989). The appearances were variable, being either solid or cystic with a nodular component, reflecting, it is thought, the degree of histological differentiation (pleomorphic, storiform, inflammatory, or myxoid) (Katenkamp, 1983). Homogeneous CT enhancement of the intracranial MFH in the present case emphasizes the varied enhancement characteristics of these tumours, as previous reports have only described heterogeneous tumour enhancement. The

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suspected dural origin of the MFH in this case is consistent with the other reported cases of primary intracranial MFH.

The presence of HCU in association with MFH is likely to be coincidental. HCU is, however, known to cause arterial and venous thrombosis which may lead to bone infarction and this has been associated with MFH (Stoker, 1986).

In conclusion MFH is a common adult soft tissue sarcoma which is rarely found in children. Intracranial MFH can occur in children, may enhance homogeneously and should be considered in the differential diagnosis of any meningeal based tumour. Localized bone destruction may prove a helpful differentiating feature from other primary intracranial tumours.

Acknowledgments

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Ultrasonic diagnosis of dislocation of the radius in an infant with Down's syndrome

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The alignment of the capitellum and the radial head is difficult to ascertain from standard radiography because they do not ossify before the age of 9 months. It may therefore not be possible to distinguish between radio-humeral dislocation and a supracondylar epiphyseal fracture in an infant (Dias et al. 1988). We report a case in which dynamic ultrasonic examination provided good definition of dislocation of the radius.

Case report

An 8-month-old infant with Down's syndrome was presented to the paediatrician when the parents noticed that the

left elbow "looked funny" at the time when the child first began to crawl. On examination the elbow was painless and a definite click could be felt when the elbow was manipulated. The head of the radius was unstable and was felt to dislocate posteriorly. The remainder of the arm appeared normal and there was no evidence of a major peripheral nerve injury. Radiographs showed no ossification of either the capitellum or the radial head and revealed normal alignment. Some deformity of the radial neck with posterior "pointing" was present (Fig. 1).

Ultrasonic examination of the elbow was performed using the 7.5 MHz curved linear array of an Aloka-630 diagnostic ultrasound machine. The elbow was scanned longitudinally

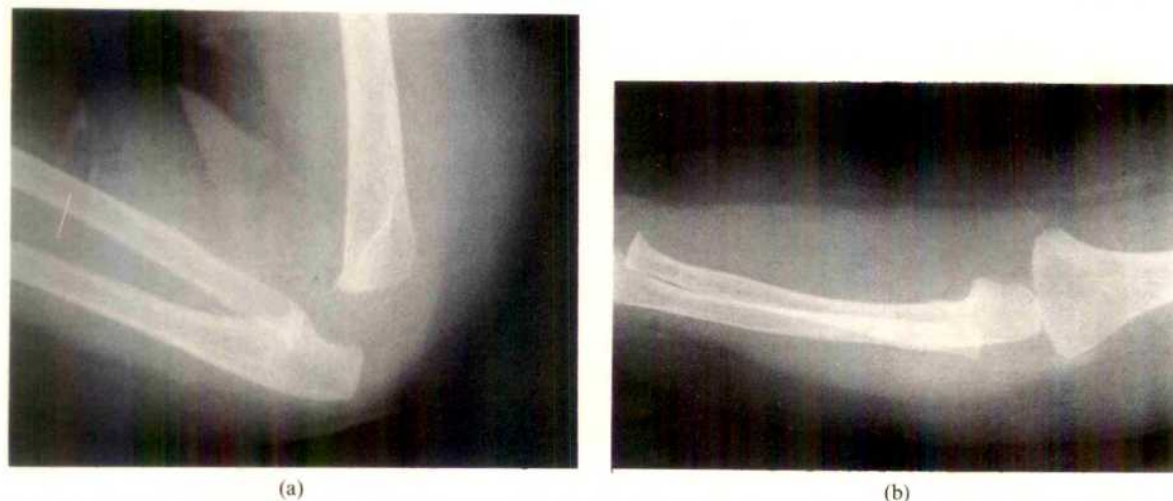


Figure 1. Lateral (a) and frontal (b) radiographs of the elbow showing apparent normal alignment of the radius and humerus. The capitellum and radial head are not ossified. There is some deformity of the radial neck with posterior pointing.

along the length of the humerus and radius from the anterior aspect (Fig. 2). Dynamic real time scanning confirmed posterior displacement of the radial head, and showed reduction of the dislocation when traction was applied to the forearm.

A decision was made not to treat the elbow operatively because of the difficulties in maintaining the reduction and the high rate of reconstruction failure in Down's syndrome.

Discussion

Dislocation of the radius without fracture of the ulna is rare in children (Sturm et al, 1989) and often associated with other abnormalities of the forearm such as

osteochondromas (Fogel et al, 1984; Masada et al, 1989) or contractures (Pletcher et al, 1976; Subbarao & Kumar, 1987). Many conditions affecting the musculoskeletal system have been associated with congenital dislocation of the radial head (Almquist et al, 1969) including familial cases (Roles, 1971; Gattley & Wedge, 1986), though some authors deny the presence of unilateral dislocation in the absence of trauma (Lloyd-Roberts & Bucknill, 1977; Mandam & Ger, 1979). In the literature we were unable to find a case of dislocation of the radial head linked to Down's syndrome. This is surprising because children with this condition

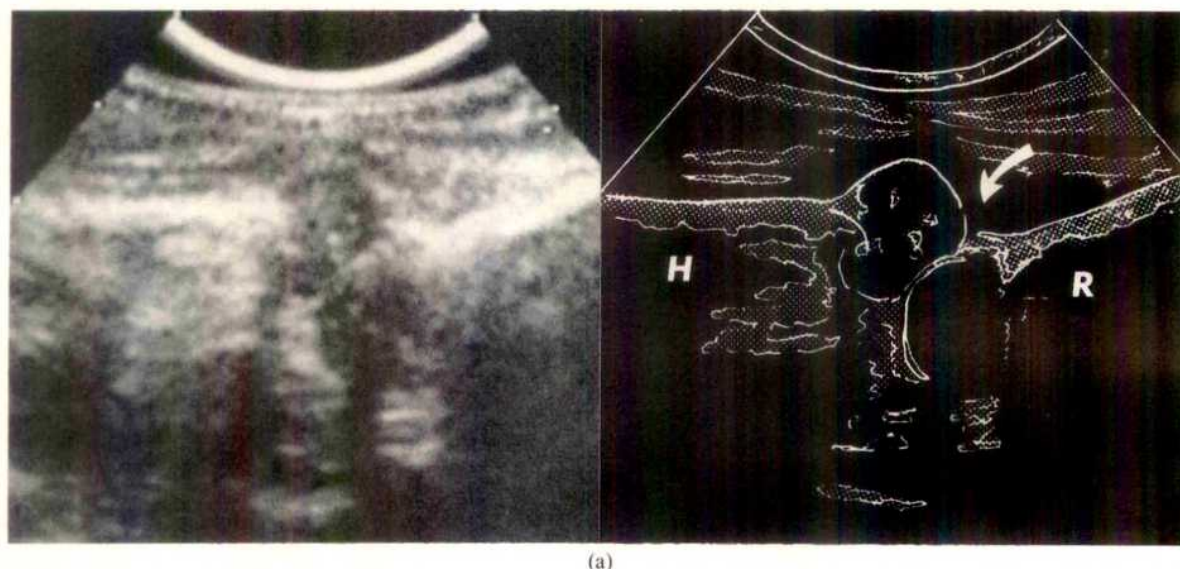
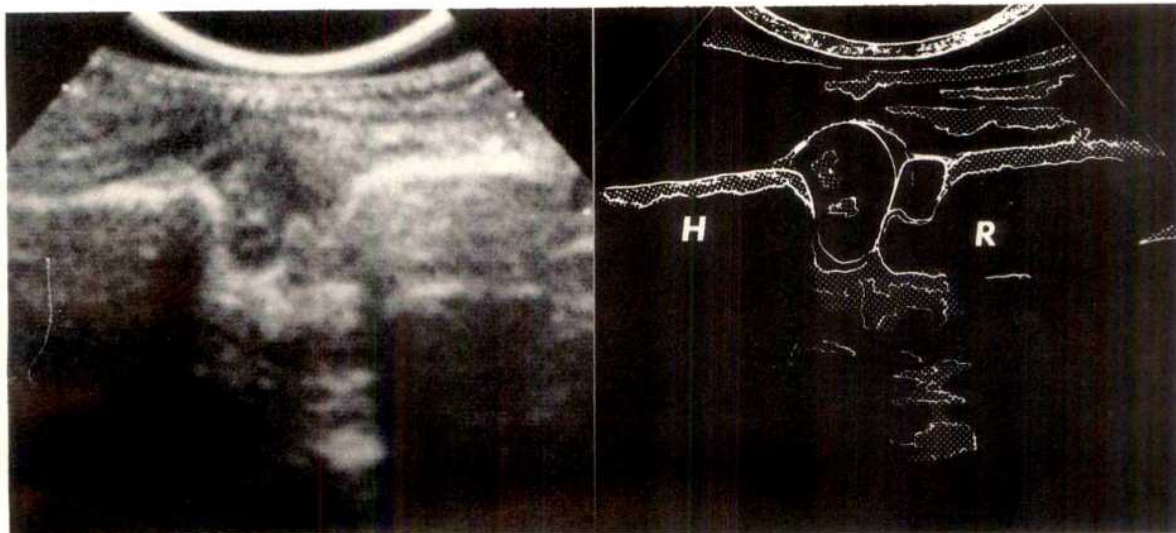


Figure 2. Anterior longitudinal ultrasound scans of the elbow (a) in neutral position, and (b) with traction applied to the forearm. Dislocation of the cartilaginous head of radius behind the capitellum can be seen in the neutral position (arrow). H & R mark the shafts of the humerus and radius.



(b)

have an increased incidence of ligamentous laxity, the most significant complication is atlanto-axial dislocation.

In this case the radiographic examination was unhelpful in confirming the diagnosis because the cartilaginous epiphyses were radiolucent and their relative position could not be ascertained. Real time ultrasonic examination, which is now well established in the examination of the infantile hip (Clark et al, 1985), clearly imaged the cartilaginous components of the elbow joint and also provided dynamic information about the dislocation. This is a non-invasive, portable technique which involves no exposure to radiation and can easily be performed in a young child.

Acknowledgment

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Melnick-Needles syndrome (osteodysplasty) in an older male—report of a case and a review of the literature

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In 1966 Melnick and Needles reported on a previously undiagnosed bone dysplasia. The diagnosis was based on characteristic radiographic findings: a delay in closure of the anterior fontanel, *i.e.* sclerosis of the skull base and mastoids. The long tubular bones are bowed with cortical irregularities and metaphyseal flaring. The ribs also show cortical irregularities and have a ribbon-like or wavy appearance. The vertebral bodies show an increase in height with a decrease in antero-posterior measurement and anterior scalloping. A decrease in disk space is also present. The pelvis has a typical constricted appearance with flaring of the iliac crest and tapering of the ischial and pubic bones. The clinical signs include exophthalmos, full prominent cheeks, mild hypertelorism, micrognathia, large ears and misaligned teeth. Females are affected almost exclusively and inheritance is in an X-linked dominant pattern. The condition is lethal in males born from Melnick-Needles syndrome (MNS) mothers (Donnenfeld, 1987). Three male patients (born from normal parents) are reported to have reached the age of 3 years.

We present the case of an 11-year-old boy, the oldest living male patient documented so far.

Case report

An 11-year-old black male presented with progressive deformity and pain in his arms, legs and chest. He was born in Angola and was the sixth of eight children (four males and four females) of healthy unrelated parents. His eldest brother was mentally retarded; the other children were normal. He was born, after a full term pregnancy, by normal delivery and the first 2 years of his life were normal. At the age of 3 he developed marked thinning of the arms. At the age of 6 his legs became similarly affected with bowing of the lower legs. He complained of fatigue and dyspnea.

On clinical examination he had a prominent and large forehead, hypertelorism and exophthalmos. His chin was small with overbite. His chest was slightly deformed with prominent

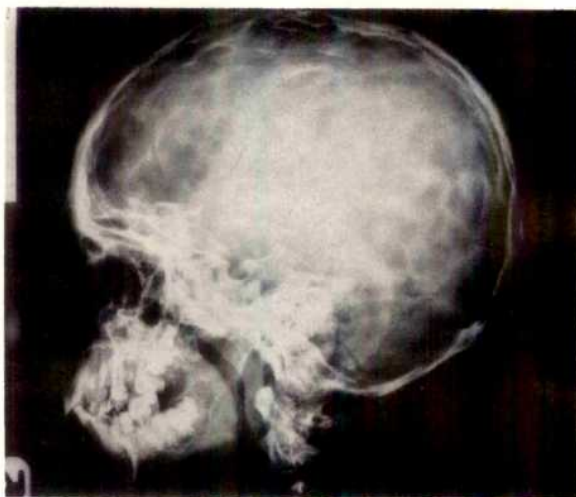


Figure 1. Lateral view of the skull.

scapular spines. His upper arms and lower legs were clearly bowed and his muscles were underdeveloped. His hands and feet were large with long fingers and toes. His weight was 26.4 kg (10th percentile, weight by stature), his height 131.5 cm (4 cm below third percentile, parental height within normal limits) and his head circumference 51 cm ($-1.4SD$). Respiration was rapid and shallow. His mental development seemed normal. Routine laboratory investigations of blood (including calcium, phosphate and alkaline phosphatase) and urine were normal. No pulmonary function tests were performed.

Radiographic findings showed that there was sclerosis of the skull base and mastoid regions, with pronounced "digital" impressions but without other signs of increased intracranial pressure, calcification in the falx cerebri, underdevelopment of the paranasal sinus, micrognathia and overbite (Fig. 1). The ribs showed cortical irregularities and a typical ribbon-like appearance. The clavicles showed medial flaring (Fig. 2). In the long bones, cortical irregularities, bowing and some metaphyseal flaring could be seen. The humeri and tibiae were especially severely affected (Fig. 3a, b), the latter having an S-shaped

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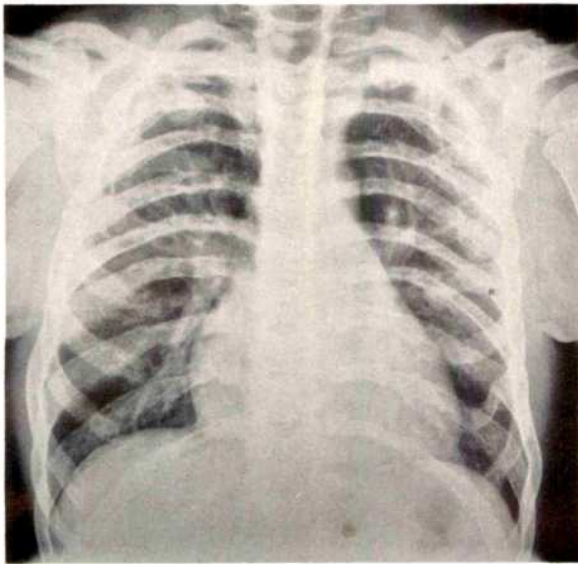


Figure 2. Thorax. Striking appearance of deformed and ribbon-like ribs.



Figure 4. The pelvis has a typical constricted appearance with flaring of the iliac crests and tapering of the ischial and pubic bones. Generalized cortical irregularity. The foramina obturatoria are small. There is coxa valga deformity and metaphyseal flaring of the femora.



(a)



(b)

Figure 3. (a) Right humerus. The proximal shaft is bowed laterally with cortical irregularities. Also the radius is bowed. (b) S-shaped configuration of tibiae.



Figure 5. Lateral roentgenogram of thoraco-lumbar spine. Anterior and posterior scalloping is present. In the lumbar region decrease of anteroposterior diameter and increase of height is evident.

configuration. Pelvic and vertebral abnormalities are shown in Figures 4 and 5.

Discussion

Considering the characteristic radiological and clinical findings in this patient, the diagnosis of Melnick-Needles syndrome is beyond doubt. It can be clearly differentiated from frontometaphyseal dysplasia; the overgrowth of the supraorbital ridge and hand abnormalities are lacking. Moreover, the irregular cortical contours and distorted appearance of ribs and tubular bones are not seen in frontometaphyseal dysplasia.

Melnick and Needles (1966) reported 13 patients with osteodysplasty of which four were males. After reviewing all published cases, Gorlin and Knier (1982) concluded that all male patients, including those published by Melnick and Needles (1966), were normal or suffering from other disorders, which made MNS a disorder limited to females.

Recently Donnenfeld et al (1987) and Krajewska-Walasek et al (1987) have reviewed all published reports of males with MNS. The condition is

lethal in the male offspring of affected females (four known cases). Viable male patients with MNS are born from healthy parents. Donnenfeld et al (1987) described a severe disorder found in males and females inherited as an autosomal recessive trait. Krajewska-Walasek et al (1987) stated that of the 13 reported living male patients 10 lacked many of the typical findings and were suffering from another syndrome (e.g. frontometaphyseal dysplasia), or should be re-diagnosed as normal. The other three had MNS. One case was added by Fryns et al (1988), which makes four cases of male patients who survived the neonatal period and had healthy parents.

Only two of these cases were still living after the age of 3 years. This present case seems to be the oldest reported living male.

Conclusion

A case of MNS in an 11-year-old black boy is described, the oldest male patient presented so far. The radiological features of male patients are not significantly different from female patients. However, female patients are otherwise healthy but male patients suffer from general bad health and die early, often from pulmonary causes. Although our patient reached the age of 11, his weight is below normal, his skeletal deformities interfere with normal movements and he complains of dyspnea. Reviewing the articles on this subject from 1966 up to the present, we conclude that the inheritance of MNS is X-linked dominant and that it is a lethal condition in males born from MNS mothers. Male patients from healthy parents should be considered as new mutations with an expression that may vary from mild to severe.

Acknowledgment

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What is it? Intraosseous lipoma in a 13-year-old boy

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Keywords: Intraosseous lipoma, Brodie's abscess

A case of intraosseous lipoma in a 13-year-old boy is presented.

Case report

This slightly obese, remarkably inactive, 13-year-old boy presented with a history of pain in the left hip over a period of 6 weeks. Besides an antalgic gait, no other abnormality was detected.

He was a product of normal pregnancy and delivery. The parents and the siblings are healthy and normal. There was no history of severe illnesses or operations. Routine blood and urine examinations were normal.



Figure 1. Plain radiograph showing a round, irregularly sclerotic lesion with single, round, radiolucent spots.

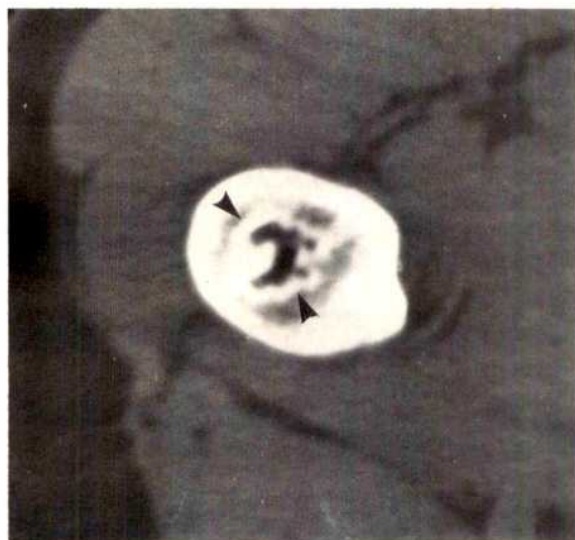


Figure 2. A CT scan of the femur shows some low-density areas with CT values compatible with fat, inside the round sclerotic lesion.

Plain radiography of the pelvis showed in the proximal part of the right femur a round, irregularly sclerotic lesion with discrete, round radiolucent spots (Fig. 1). Computed tomography (CT) an H-shaped radiolucency that had a sclerotic, thick rim. The CT values of the radiolucent lesion were compatible with fat (Fig. 2).

Discussion

Osseous lipoma is one of the rarest primary bone tumours in adults. Dahlin & Unni (1986) quote an incidence of 1 per 1000 cases. Only single cases of bone lipoma have been reported in childhood. In a review of the literature over a span of 100 years, Hart (1973) found 28 cases reported up to 1969; four of these were children. Ramos et al (1985) regard osseous lipoma as the most rarely encountered benign neoplasm of bone with approximately 60 cases reported up to 1985. In two recent papers with 14 cases of bone lipoma the youngest patient was 30 years old (Milgram, 1981; Ramos et al, 1985).

Bony lipoma presents as a paraosseous or intraosseous lesion. The former is two to three times more

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common than the latter. Occasionally congenital bone abnormalities are associated with deep, soft-tissue lipoma (Sauer & Ozonoff, 1985). Although intraosseous lipoma may occur in any bone, the proximal femur, calcaneus, fibula and ribs are most frequently affected. The preferred site in the long bones is the metaphyseal region. Depending on the size and location of the tumour it may be asymptomatic or may cause mild, localized pain and swelling (Carulo & Dahlin, 1953; Mueller & Robbins, 1960; Hart, 1973; DeLee, 1979; Milgram, 1981; Ramos et al, 1985; Schajowicz, 1981).

Similarly the radiographic appearances of intraosseous lipoma depend on size and location of the tumour. Usually it presents as a lytic, well circumscribed lesion without significant cortical erosion and without periosteal reaction. Only in rare instances does a large intraosseous lipoma show malignant features (Carulo & Dahlin, 1953). In narrow bones, such as the fibula and ribs, intraosseous lipoma presents as an expansile lesion. In some cases—as in our patient—a reactive sclerotic border around the lytic lesion is observed. This radiographic pattern is said to be characteristic for proximal femoral lesions localized in proximity to the intertrochanteric line (Ramos et al, 1985).

Histologically the tumour presents as regular lobules of mature adipose tissue with bony trabeculae within the lesion (DeLee, 1979; Downey et al, 1982).

The X-ray differential diagnosis of our patient includes all the single radiolucent lesions—simple bone cyst, aneurysmal bone cyst, eosinophilic granuloma, intraosseous enchondroma, fibrous dysplasia, chondromyxoid fibroma, metastases and Brodie's abscess (Kozlowski, 1980). Although all of them may be asymptomatic at the early stages of development a thick, sclerotic border is unusual for any of them.

Low CT values compatible with fat were observed in reparative osteomyelitis due to histiocytes laden with fat vacuoles (Ramos et al, 1985). Brodie's abscess in childhood is usually located in the metaphysis and in rarer instances in the epiphysis. The metaphyseal location is

characterized by adjacent growth cartilage localization. We did not see any case of asymptomatic Brodie's abscess in children. There were no signs or symptoms suggesting this diagnosis in our patient.

The practical importance of this case is that not every strange-looking, unusual bony lesion needs further investigations after proper radiographic imaging has been performed. The conclusion is that this clinically and radiologically benign tumour belongs to the "leave me alone" group of lesions and bone biopsy is unnecessary.

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Post-mastectomy lymphangiosarcoma (Stewart-Treves syndrome): report of two long-term survivals

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Lymphangiosarcoma is one of the rarest forms of soft tissue neoplasms. Lowenstein (1906) was the first to report this entity in a patient with chronic post-traumatic upper extremity lymphoedema. However, it was not until Stewart and Treves (1948) described the development of this malignancy in a post-mastectomy oedematous extremity that this syndrome, which carries their name, became widely recognized.

The tumour is highly malignant and usually arises in a lymphoedematous upper extremity of a patient treated for carcinoma of the breast. It has been well established that lymphangiosarcomas are not directly related to breast cancer (Aegerter & Peale, 1942). The common denominator is the lymphoedema and, therefore, other causes of chronic lymphoedema may lead to the development of this vascular sarcoma (Taswell et al, 1962). Indeed, this disease has occurred in congenital (Dubin et al, 1974), idiopathic, traumatic and filarial lymphoedema (Devi & Bahuleyan, 1977). The pathogenesis of these unusual tumours remain uncertain. Stewart and Treves (1948) believed that a systemic carcinogen was involved in the etiology. Martorell (1951) suggested that the lymphoedema may be tumour inducing while Schreiber et al (1979) postulated that local immunodeficiency was the causative factor.

Histologically these tumours consist of large vascular cavities lined with plump, spindle-shaped endothelial cells containing large nuclei and prominent nucleoli. Some areas may exhibit solid sheets of spindle cells (Silverberg et al, 1971). Immunohistochemistry may prove to be quite useful; factor VIII-AG is the most utilized marker for vascular differentiation (Mukai et al, 1980).

Lymphangiosarcomas affect all races including blacks (DiSimone et al, 1970), orientals (Tomita et al, 1978) and caucasians. The median time from mastectomy to the development of lymphangiosarcomas is 10 years (Woodward et al, 1972), ranging from 5 (Yap et al, 1981) to 27 years (Enzinger & Weiss, 1988). The average

age of patients is about 62 years (Southwick & Slaughter, 1955).

In a review of 894 women who survived 5 years following radical mastectomy with or without radiation therapy, Shirger (1962) reported an incidence of Stewart-Treves syndrome of 0.45%. Fitzpatrick (1969), however, encountered only 7 patients (0.07%) who developed lymphangiosarcoma when he reviewed the records of 9000 patients treated with mastectomy. All seven had had adjuvant radiation therapy. He noted that lymphoedema was a complication more likely to follow Halsted's operation as compared with less radical surgery and he stated that the risk of lymphoedema increased if the axilla was irradiated. Since lymphangiosarcoma is a rare disease, most reports consisted of a small number of patients. By 1972, approximately 200 cases of lymphangiosarcomas complicating chronic lymphoedema had been recorded in the world literature (Woodward et al, 1972).

Clinically the tumour appears as bluish, purplish, reddish skin nodule(s) on a lymphoedematous arm. These lesions tend to grow, coalesce, ulcerate and spread proximally and distally to involve the entire arm. The disease also tends to metastasize through the blood stream to distant organs, particularly the lung. Treatment of extremity lymphangiosarcoma includes local excision, wide excision, amputation, radiation therapy, chemotherapy, and combined methods (Southwick & Slaughter, 1955; Chu & Treves, 1963; DiSimone et al, 1970; Yap et al, 1980; Sordillo et al, 1981; Yap et al, 1981). The prognosis is poor, as most patients die within 5 years of diagnosis despite various forms of treatment. The median survival is about 2.5 years (Sordillo et al, 1981) with very few long-term survivals.

The purpose of this report is to describe two patients with Stewart-Treves syndrome who survived at least 13 and 19 years following combined modality treatment. They were among the first patients with this condition to be treated with Actinomycin D chemotherapy and radiation therapy, with curative intent.

Case reports

Case 1

The patient was a 66-year-old white female who underwent a left radical mastectomy in 1952 for infiltrating duct carcinoma

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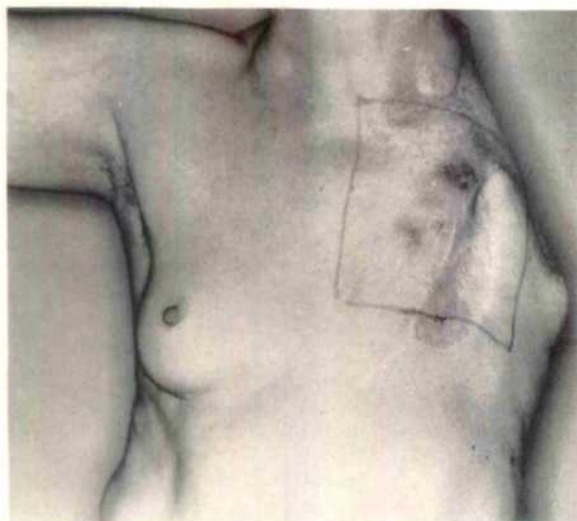


Figure 1. Recurrent lymphangiosarcoma involving the left anterior chest wall near the amputation stump.

with metastases to the axillary lymph nodes. She received a course of post-operative radiation therapy, details of which were unavailable. Shortly after surgery the patient developed left arm lymphoedema.

In September 1966 she noticed induration and pain throughout her left arm and, 2 weeks later, numerous bluish skin nodules appeared; biopsy showed lymphangiosarcoma. It was decided to treat the patient with a left interscapulo-thoracic amputation combined with Actinomycin D chemotherapy. The first dose of Actinomycin D, 2 mg intravenously, was administered 6 days prior to surgery and her second dose was on November 30, 1966, the day of surgery. Her surgical specimen demonstrated lymphangiosarcoma present in multiple subcutaneous nodules and diffusely in the dermis. The margins of resection were free of tumour.

2 months later two purplish skin nodules were noted on her left anterior chest wall (Fig. 1). Biopsy again demonstrated lymphangiosarcoma (Fig. 2). The patient was referred for radiation therapy which was started on February 27, 1967.



Figure 2. Anastomosing irregular vascular channels, lined by atypical endothelial cells (Haematoxylin and Eosin stain, $\times 69$).

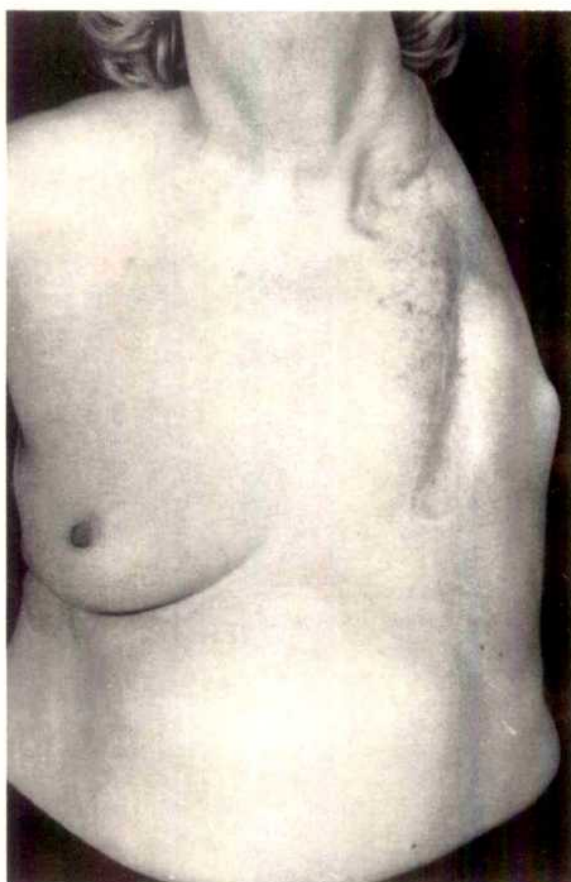


Figure 3. Photograph taken 12 years after radiation therapy and Actinomycin D for recurrent disease. Patient was alive and well 19 years post combined treatment.

Using a single portal measuring 15×15 cm, the left anterior chest wall was irradiated to a total dose of 5500 cGy in 27 fractions over 31 elapsed days, using a 6 MeV electron beam. The two nodules received an additional boost dose of 500 cGy, delivered in 2 fractions in 4 days through a reduced field.

3 weeks later a small new lesion was noted at the upper border of the radiation field. This was treated with a 3.5 cm circular field to a total dose of 3200 cGy in 16 fractions delivered in 3 weeks, using 6 MeV electron beam. All three nodules disappeared following therapy.

The patient again received Actinomycin D chemotherapy, 2.0 mg intravenously monthly, from May 12, 1967 until October 30, 1970, which she tolerated well. She was last seen in 1985, 19 years after radiation treatments; she was without any evidence of recurrent lymphangiosarcoma (Fig. 3). Since the patient resides in Sweden, there has been no further follow-up.

Case 2

The patient was a 66-year-old white female who had undergone a right radical mastectomy in 1962, at the age of 37, for infiltrating duct carcinoma with negative axillary nodes. She received no adjuvant radiation therapy. Lymphoedema of the right arm was noted shortly after mastectomy. In 1977, 15 years following the radical mastectomy, a small bluish,

purplish, flat lesion was noted on the lateral aspect of her right arm. Incisional biopsy revealed lymphangiosarcoma and the patient was referred for radiation therapy.

Since lymphangiosarcoma tends to have extensive local involvement, it was planned to irradiate a wide area of the arm. The lateral aspect of the arm was treated first. A total dose of 5400 cGy was delivered in 27 fractions over 44 elapsed days, using a 15 MeV electron beam. This was followed by irradiation of the medial aspect of the right arm and a total dose of 5000 cGy in 25 fractions was delivered over a period of 36 days. A narrow, longitudinal strip of the arm was spared in order to preserve adequate lymphatic drainage.

Since Case 1 had done so well with Actinomycin D, the same drug was administered to Case 2 after completion of radiation therapy. She received Actinomycin D, 2.0 mg intravenously, once weekly for 3 consecutive weeks, followed by a 2 week rest period. Maintenance therapy continued from April 1978 to November 1979.

The patient remained in good health until December 1988 when she developed carcinoma of the opposite breast. She underwent a left modified radical mastectomy and the pathology was infiltrating duct carcinoma with negative axillary lymph nodes. She was last seen in September 1990. 13 years after treatment there was no evidence of recurrent lymphangiosarcoma and she was also free of breast cancer.

Discussion

Lymphangiosarcoma is an aggressive cancer with a rapidly progressing clinical course. McConnell and Haslam (1959) described three phases of development of post-mastectomy lymphangiosarcomas, *i.e.* prolonged lymphoedema, angiomatosis and, finally, angiosarcoma. However, overlapping among the three phases is possible. Chu and Treves (1963) suggested that longer survival might be associated with the diagnosis in early phases. The importance of early recognition of a suspicious bluish, reddish lesion on a lymphoedematous arm, immediate biopsy and prompt treatment cannot be overemphasized.

Lymphangiosarcoma occurs in a lymphoedematous extremity. Prevention of lymphoedema would logically lower the incidence of the development of lymphangiosarcoma. During the past few decades, there has been a definite trend toward performing less radical surgery in the treatment of breast cancer. Modified radical mastectomy and partial mastectomy have largely replaced the classical Halsted radical mastectomy, because the survival results are similar with reduced morbidity including the incidence and severity of lymphoedema of the arm. Although no survey regarding the frequency of lymphangiosarcoma in currently treated patients has been available, it is our clinical impression that we are seeing less numbers of patients inflicted with this disease in recent years.

Management strategies include surgery, radiation therapy and chemotherapy. Surgical treatment should consist of either wide excision or amputation. Sordillo *et al* (1981), in a review of 44 cases seen at the Memorial Hospital, New York City, reported a median survival of 48 months in 11 patients treated with amputation, as compared with 20 months median survival in other patients with radiation therapy or chemotherapy.

However, the numbers of cases were relatively small so no firm conclusion can be made regarding the efficacies of various treatments.

Radiation therapy has been used frequently for adjunctive, curative or palliative treatments. Lymphangiosarcomatous lesions do respond to radiation therapy (Southwick & Slaughter, 1955; Chu & Treves, 1963; DiSimone *et al*, 1970) with an occasional cure. Since lymphangiosarcoma is usually a multifocal disease with extensive clinical or subclinical involvement, radiation therapy should play a major role in its management. We recommend wide-field technique, even when the lesion may appear to be small and limited, and high doses of radiation of the order of 5500 to 6000 cGy delivered in 27–30 fractions over a period of about 6 weeks. This would mean treating practically the entire arm, sparing only a narrow longitudinal strip of skin to preserve lymphatic drainage. An example of the wide-field technique can be seen in the treatment of Case 2 whose lesion appeared to be clinically solitary.

Chemotherapy is a relatively new method of treatment compared with surgery and radiation therapy, so our experience regarding its efficacy in lymphangiosarcoma is extremely limited. It is also difficult to determine which regimen is more effective, since lymphangiosarcoma is a rare disease and very few patients are available for study.

Yap *et al* (1981) reviewed 22 patients seen at M. D. Anderson Hospital for post-mastectomy lymphangiosarcoma over a 20 year period. 13 patients were treated regionally or systemically or both, with a variety of single or combination chemotherapeutic agents; the overall response rate was 42%. Five patients who failed to respond to chemotherapy had a median survival of 4 months, whereas the six chemotherapy responders had a median survival of 26.5 months.

Our two cases of long-term survival were managed with high doses of radiation therapy and Actinomycin D. Case 1 was actually an amputation failure and the two doses of Actinomycin D, given before and during surgery, were inadequate to prevent recurrence. However, the recurrent disease was salvaged by a combination of radiation therapy and Actinomycin D. The excellent results may suggest that chemotherapy and radiation therapy have additive or synergistic effects. Our first patient was treated 24 years ago and the second 13 years ago. At that time Actinomycin was the drug of choice for these two patients. More recently, the most frequently used agent for treatment of vascular sarcomas is doxorubicin (Adriamycin), either alone or in combination with other agents.

We recommend close follow-up of all patients with post-mastectomy lymphoedema of the arm. Biopsy of any suspicious lesion should be carried out without delay. Aggressive management with surgery, radiation therapy and chemotherapy may offer an optimistic outlook if the neoplasm is discovered in its early phases. Our experience with these two patients showed encouraging results with a combination of radiation therapy and Actinomycin D treatments.

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Acute epidural haematoma complicating myelography in a normotensive patient with normal blood coagulability

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Acute epidural haematomas are usually idiopathic, but they may occur following spinal trauma (Coin et al, 1979), epidural anaesthesia (Helperin et al, 1971) or in association with spinal tumours (Harris et al, 1978) or vascular malformations (Muller et al, 1982). We report the computed myelographic, computed tomographic

(CT) and magnetic resonance imaging (MRI) findings in an unusual case complicating lumbar myelography, requiring surgical decompression, which was not evident on the myelogram.

Case report

A 75-year-old woman with chronic low back pain and sciatica presented with increasingly severe right leg and buttock pain. This had developed after surgery for an L4/5 spondylolisthesis and spinal canal stenosis 2 years previously. In 1984 she had an

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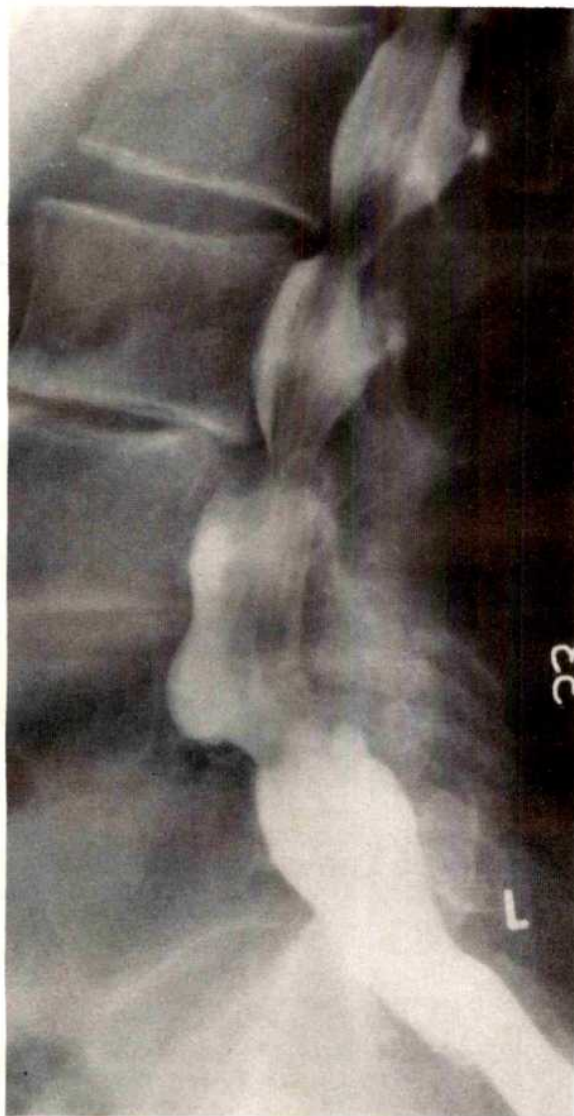


Figure 1. Lateral view of the water-soluble myelogram.

L4/5 dissection for left leg and buttock pain with no lasting benefit. She was unable to walk because of pain, ankle jerks were absent and there was limited straight leg raising on the right. She was normotensive and there was no evidence of blood dyscrasia or clotting abnormalities.

Plain radiographs of the lumbar spine showed complete resorption of the L4/5 intervertebral disc with a Grade II spondylolisthesis, and mild retrolisthesis of L1, L2 and L3. A myelogram was performed with a 22 gauge disposable needle at the L1/2 interspace with the patient sitting. When clear cerebrospinal fluid (CSF) was obtained she was laid on her side and 12 ml of iohexol (240 mg/ml) introduced under fluoroscopic control. A posterior nuclear herniation was shown at L2/3, and a small posterior protrusion at L1/2. At L2/3, the theca was deformed from the right with prominent posteromedial deviation of the right L3 root (Fig. 1). Computed tomography 30 min later showed a large left posterolateral intraspinal mass at

the level of L1 and L2; the L2/3 nuclear herniation was not visualized (Fig. 2).

Soon after the myelogram the patient began to complain of increased pain in the back and severe left leg pain, and over the next 2 h she became unable to move the left leg. There was marked reduction in power of the left leg without change in tone or reflexes. The patient's condition stabilized but did not improve, and 2 days after the myelogram a second CT scan showed the mass to be slightly denser than CSF. Magnetic resonance imaging performed at 1.5 T showed a tapered intraspinal mass posterior to the theca at L1 and L2, which returned a signal greater than CSF on T_1 -weighted spin-echo images, and very low signal on T_2 -weighted images, establishing that it was a recent haematoma. A large nuclear herniation from the L2/3 intervertebral disc extended inferiorly on the right (Fig. 3).

By the third day there was still no improvement, and a wide laminectomy was performed from L1 to L3. A large, firm epidural haematoma closely applied to the dura mater was removed. Within 24 h of the operation the patient began to recover power in the left leg.

Discussion

Most reported spinal epidural haematomas are spontaneous and acute (Post et al, 1982; Zilkha et al, 1983; Beatty & Winston, 1984; Haykal et al, 1984; Rothfus et al, 1987; Williams & Nelson, 1987; Avrahami et al, 1989; Laissy et al, 1990), usually occurring in elderly men, over half of whom have been hypertensive or on anti-coagulant therapy. The cervical, thoracic and lumbar spine are affected in decreasing order of frequency; most haematomas are posterolateral, but a few have been lateral or anterolateral (Leviton & Wiens, 1983). Most extend over at least two vertebral segments, though uncommonly over more than three or four. They usually present acutely with severe pain, sensory disturbance and paresis, but chronic presentations are documented (Leviton & Wiens, 1983). Approximately 70% of cases reported since 1982 have been treated by operative decompression, the remainder being diagnosed by modern imaging methods and successfully managed conservatively (Avrahami et al, 1989; Laissy et al, 1990). Controversial aspects include the source of spontaneous haemorrhage, from epidural arteries (Beatty & Winston, 1984; Rothfus et al, 1987), veins (Helperin & Cohen, 1971; Post et al, 1983) or occult vascular malformations (Solero et al, 1980; Muller et al, 1982), and the mechanisms of containment in the epidural space which result in a compressive mass sufficient to cause severe neurological dysfunction (Helperin & Cohen, 1971; Beatty & Winston, 1984).

Large epidural haematomas sufficient to contribute to neurological dysfunction are uncommon in spinal trauma. Occasional examples have been reported following both blunt and penetrating injuries (Coin et al, 1980), usually in the cervical region. A haematoma similar in extent and location to our case following epidural anaesthesia was shown by oil myelography (Helperin & Cohen, 1971), and others have occurred after lumbar disc removal (Di Lauro et al, 1982). Intraspinal haemorrhage is a recognized complication of lumbar puncture and myelography (Post et al, 1982), and examples have been reported in elderly patients who

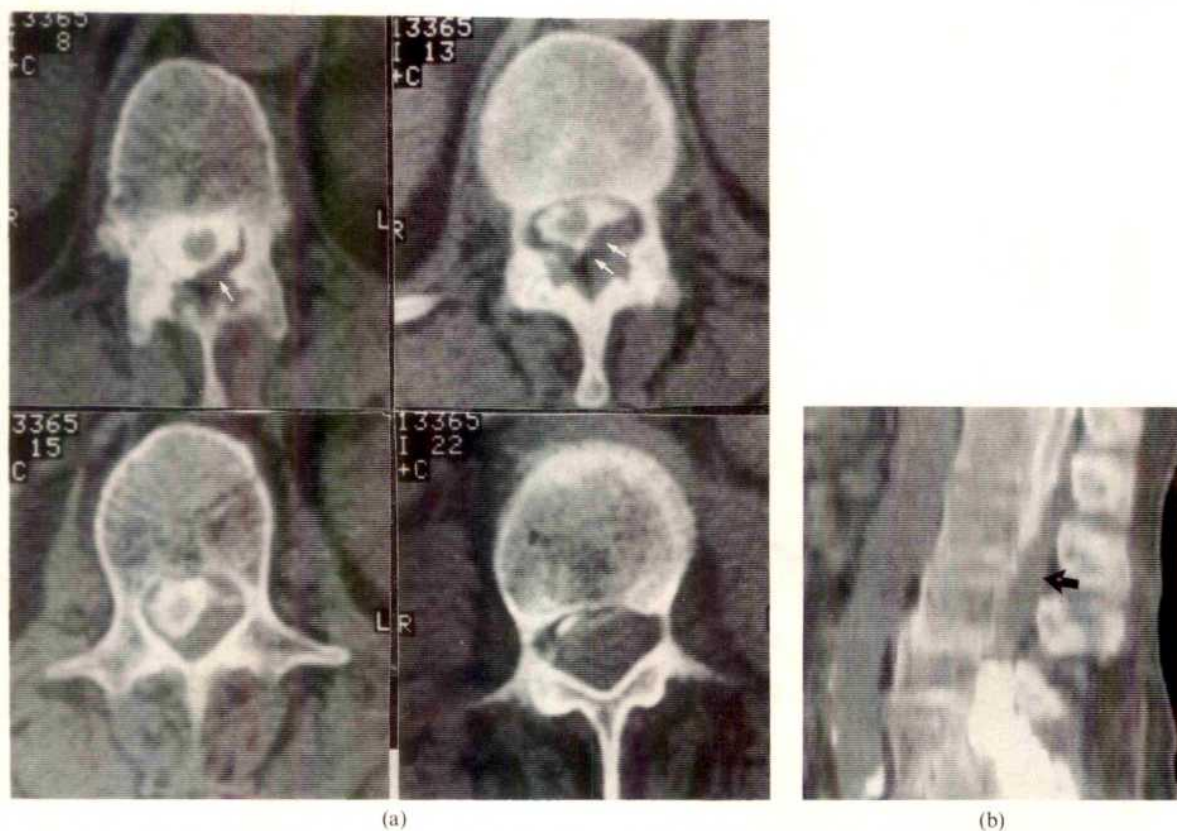


Figure 2. Post-myelography CT scans. (a) Selection of axial images, showing apparent thickening of the ligamentum flavum (double arrows), dura mater (single arrow), and large mass occupying almost the entire spinal canal. (b) Mid-sagittal reformatted image showing the large epidural mass (arrow).

are hypertensive, thrombocytopenic or on anticoagulant therapy (Edelson et al, 1974; Kirkpatrick & Goodman, 1975; Brem et al, 1981); the risk is increased in repeated lumbar punctures and after a traumatic tap (Post et al, 1982). However, at least in recently documented cases, bleeding following lumbar puncture has been subdural or subarachnoid; we could find no reported case of a purely epidural haematoma complicating myelography, documented by modern imaging methods. The precise mechanism in our case remains a matter for speculation, although relationship to the needle traversing the epidural space is inescapable. It is unlikely that transfixing epidural veins with a 22 gauge needle would be sufficient, and tearing of loosely supported epidural veins or arteries seems more probable. This may have occurred as the patient was moved from the sitting to the decubitus position and movement of the needle in the epidural space may have been accentuated by the vertebral subluxations. That the extradural mass did not become apparent during the 5–10 min required to complete the myelogram, but was apparent on CT approximately 30 min later, probably attests to venous rather than arterial bleeding.

The appearance of the epidural haematoma in this

case was similar to that described in spontaneous examples. Discriminatory signs on computed myelography, well seen in our patient but not emphasized in existing literature, were: (i) apparent thickening of the ligamenta flava on the side of the lesion, presumably due to juxtaposed clot (Rothfus et al, 1987); and (ii) a dural tail extending from the tapered superior and inferior margins of the haematoma closely resembling localized dural thickening, presumably representing dural-based clot dissecting a plane between dura and epidural fat (Williams & Nelson, 1987). These features are unusual, and when present in combination may be specific. The differential diagnosis lay between synovial cyst, large migratory nuclear fragment, extradural arachnoid cyst or intraspinal tumour. Given the shape and extent of the lesion and its delayed appearance only a cyst of varying size seemed relevant, and could have been supported by appearances on the second CT scan had they been interpreted as indicating delayed penetration and retention of contrast medium within the cyst.

Magnetic resonance imaging provided an unequivocal pre-operative diagnosis. The relatively high signal on T_1 -weighted images (Rothfus et al, 1987; Avrahami et al, 1989) and low signal on T_2 -weighted images (Avrahami

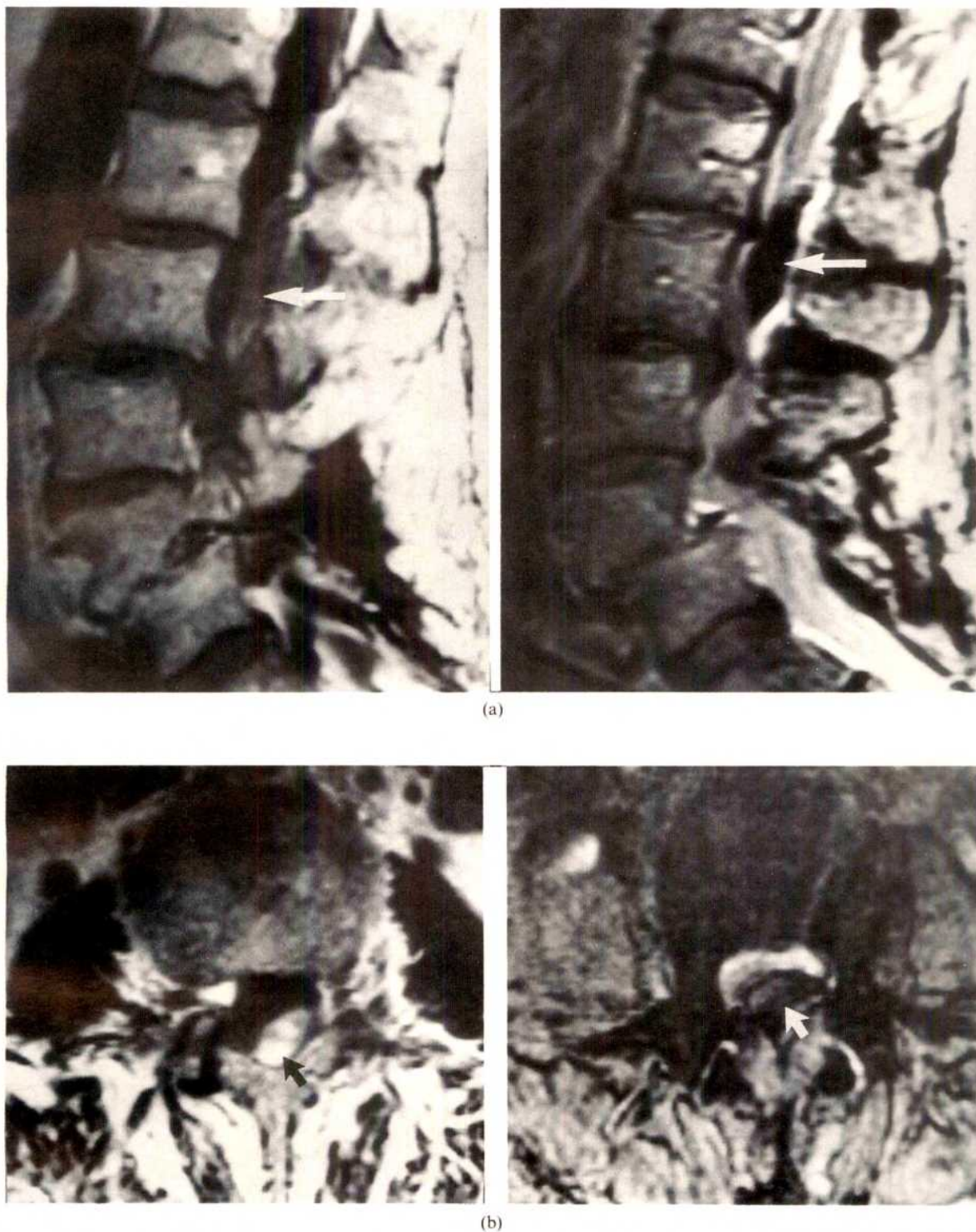


Figure 3. Magnetic resonance images. (a) Sagittal, left TR 500, TE 10; sagittal right TR 1846, TE 30 (256 × 128 matrix). The haematoma is indicated by arrows; signal from it was even lower on the later echo (TE 80). (b) Axial, left, spin-echo TR 600, TE 13; axial, right, gradient echo (GRASS) TR 840, TE 23, flip angle 20°. The level is L2. High signal on T_2 -weighted images and relatively low signal on T_2^* -weighted gradient echo sequences are clearly shown (arrow). Note also that the lateral margins of the haematoma are rounded rather than tapered.

et al, 1989) were typical. The inhomogeneous low signal on gradient echo images at a flip angle of 20° was different from that in the case of Avrahami et al, but this probably reflects the younger age of the clot in our case.

It is clear that not all epidural haematomas require operation. Many cases have been managed conservatively and have completely recovered (Laissy et al, 1990). Usually, however, the catastrophic presentation prompts early operative intervention, and undue delay may result in less chance of complete recovery (Post et al, 1982; Beatty & Winston, 1984). Because the neurological findings in our patient were confined to a previously symptomatic part and tended to fluctuate in severity, operation was delayed until it was clear that no substantial recovery in left leg function was occurring. Post-operative recovery was almost complete by 1 week.

Intraspinal haemorrhage is a rare complication of myelography. This case shows that although it may not be recognizable at the time of the myelogram, it can still be a cause of subsequent clinical deterioration requiring active intervention.

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Spinal cord compression in Paget's disease due to extradural pagetic ossification

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Neurological complications resulting from single vertebral involvement have been described but the condition is usually asymptomatic (Dinneen & Buckley, 1987).

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The mechanisms for neurological involvement include compression of the spinal cord by bony expansion from the pagetic process, vertebral collapse with haemorrhage, or neoplastic degeneration (Resnick, 1988). Other non-compressive vascular causes have also been described (Herzberg & Bayliss, 1980; Douglas et al, 1981).

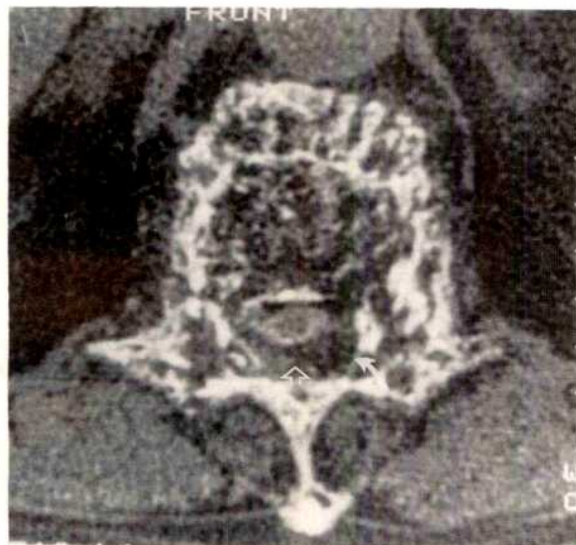


Figure 1. CT through lower body of L1 showing mixed osteolytic and osteoblastic Paget's disease affecting the entire vertebral body and neural arch. The bony spinal canal is normal (curved arrow). The extradural fat contains regions of high density (open arrow) and the theca is compressed by it.

We describe a case of severe spinal cord compression secondary to Paget's disease, as a result of extradural pagetic ossification of the ligamentum flavum and epidural fat, with the actual bony spinal canal being of normal size.

Case report

A 73-year-old man, blind for many years due to glaucoma, with known Paget's disease of bone was admitted as an emergency with a 3 month history of low back pain, progressive numbness and weakness of both legs and increasing loss of perianal sensation. His gait had become uncoordinated and his severe walking difficulties were compounded by his blindness. On examination the abnormalities were confined to the nervous system. The upper limbs were normal but in the legs there was a spastic paraparesis with a generalized increase in muscle tone and moderate decrease in power in all muscle groups. Proprioception and vibration sense were absent and there was decreased perception of light touch below T10, most marked distally. Pin prick sensation was dulled below the knees and perianally.

Routine haematological and biochemical screening was normal apart from an alkaline phosphatase of 1410 iu (normal range 25–110) and an ESR of 78 mm/h. Serum immunoglobulins were normal and no light chains were detectable in the urine. Radiographs showed extensive Paget's disease of the pelvis and L1 vertebral body. Myelography demonstrated a complete extradural block at the lower border of L1 level adjacent to the diseased vertebral body. Post-myelographic computed tomography (CT) showed high density regions in the epidural fat causing compression of the theca at L1 level (Fig. 1). A provisional diagnosis of spinal cord compression due to Paget's disease affecting the L1 vertebrae was made with the possibility of an associated epidural haematoma or sarcomatous change. Intramuscular calcitonin (100 units daily) was given for 5 days pre-operatively in an attempt to reduce the

vascularity of the bone, and resulted in a fall in the alkaline phosphatase level to 845 iu. At operation, surgical decompression was undertaken with deroofting of the spinal canal down to the dura. The L1 vertebra was replaced by pagetic bone and extensive extradural greyish soft tissue was present. The ligamentum flavum was adherent to the epidural fat which itself appeared partly calcified and fixed to the dura. This extradural tissue was dissected from the dura and it became apparent that the spinal stenosis was as a result of this extensive band of extradural tissue.

Histological examination confirmed Paget's disease of the L1 vertebral body. The greyish extradural tissue consisted of fibroadipose with multiple areas of pagetic bone activity with fragments of bone metaplasia and multinucleated giant cell osteoclasts. In some areas faint cement lines formed a mosaic-like pattern. The ligamentum flavum showed areas of non-calcified and calcified bone fragments. There was no evidence of either haemorrhage or malignancy in the specimen. Post-operatively there was gradual improvement in the power of the lower limbs over several weeks, but the sensory abnormalities remained unchanged. Subsequently, he was treated with a course of intermittent intravenous APD (3-amino-1-hydroxypropylidene-1,1-bis-phosphonate), at 2 weekly intervals for 12 weeks and his alkaline phosphatase fell further to 250 iu. The patient is now at home and is mobile, with the aid of a frame.

Discussion

Paget's disease of bone is a condition of unknown cause that affects approximately 3–4% of the population over the age of 40 years. It affects men more often than women, with the age of onset being slightly lower in men. Although variable in its clinical manifestations, Paget's disease is asymptomatic in most instances. The disease affects more than one bone in 75–90% of cases (Hamdy, 1981), with the most common sites in the spine being the sacrum followed by the lumbar spine (Schmorl & Junghans, 1959). The musculoskeletal complications of Paget's disease include osseous deformities, fractures, neoplasms, soft-tissue masses, osteomyelitis, extramedullary haematopoiesis, crystal deposition, degenerative joint disease and neurological abnormalities. Paraparesis is a well recognized but uncommon complication secondary to Paget's disease of the vertebral column, with approximately 100 cases being recorded since it was first reported by Wyllie (1923). Paraparesis is most common with dorsal involvement due to the already small calibre of the spinal canal.

This patient's myelographic findings were consistent with a severe degree of subarachnoid block resulting in spinal cord compression. CT demonstrated the cause to be due to ossification of the epidural fat and ligaments with associated Paget's disease of the L1 vertebra. The appearances raised the possibility of associated epidural haematoma, as previously described (Hanna et al, 1989), or sarcomatous change with extension into the extradural space, and hence surgery was undertaken.

Previously, CT has shown that spinal cord compression in Paget's disease occurs as a result of expansion of the vertebral body or neural arch into the spinal canal (Weisz, 1983; Zlatkin et al, 1986). Additional mechanisms that have been proposed include a vascular steal phenomenon by pagetic bone and direct compression of

the anterior spinal artery (Walpin & Singer, 1979; Herzberg & Bayliss, 1980). Ossification of the extradural soft tissues causing cord compression, as in this case, is a very rare occurrence with only a few isolated case reports (Clarke & Williams, 1975; Hadjipavlou et al, 1988).

In the past the only effective treatment for spinal cord compression secondary to Paget's disease has been surgical decompression. More recently medical treatment with calcitonin and diphosphonates have proved effective in the treatment of Paget's disease (Singer, 1977), as well as being successful in the management of paraparesis associated with Paget's disease (Melick et al, 1976; Walpin & Singer, 1979). It is now being suggested that the results of medical treatment are as good as, if not better than, those obtained with surgical intervention, especially when multilevel disease is present (Jawad & Berry, 1987) and when there is early institution of therapy (Craig & Hodkinson, 1985). Surgical decompression was performed in this patient to confirm the etiology of the unusual appearance of the extradural tissue demonstrated on CT.

CT is useful in the diagnosis of Paget's disease as well as for the assessment of spinal stenosis and its possible cause. Patients with radiographic evidence of Paget's disease and with clinical symptoms of cord involvement benefit from early CT assessment of their disease to aid in a rational approach to therapy (Zlatkin et al, 1986). This case demonstrates the value of post-contrast CT by allowing better visualization of the subarachnoid space and the unusual cause of the spinal cord compression.

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Case of the month

A pain in the neck!

By R. Rajah, FRCS, FRCR, A. Boothroyd, FRCR and W. R. Lees, FRCR

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(Received April 1990)

A 36-year-old female presented with a 24 h history of constant severe pain in the left side of her neck. On clinical examination there was marked tenderness and swelling within the left anterior triangle of the neck. She had documented polycystic ovarian disease and her two previous pregnancies were induced by Clomiphene and an LHRH pump, respectively. 2 months prior to this presentation she had received 10 000 u of human chorionic gonadotrophin (HCG) and her ovaries were monitored regularly. 3 weeks later she developed abdominal distension, nausea, weight gain, pleural effusion, low blood pressure and a tachycardia. A frontal chest radiograph was taken (Fig. 1). At this stage a clinical diagnosis was made and treatment commenced. 3 weeks later she presented with neck pain and an ultrasound examination was performed (Fig. 2a & b) using 5 MHz linear probe.

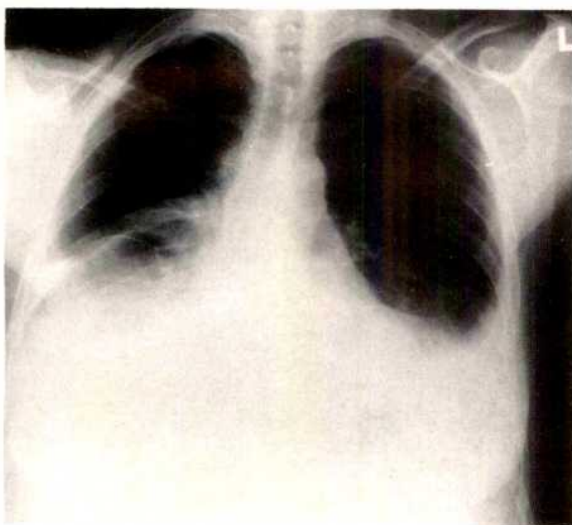
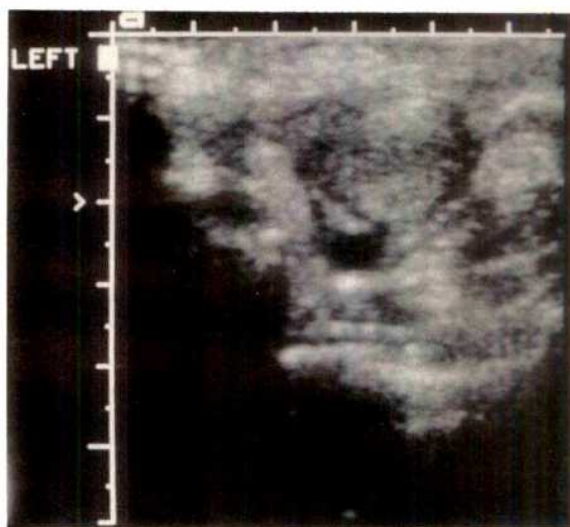


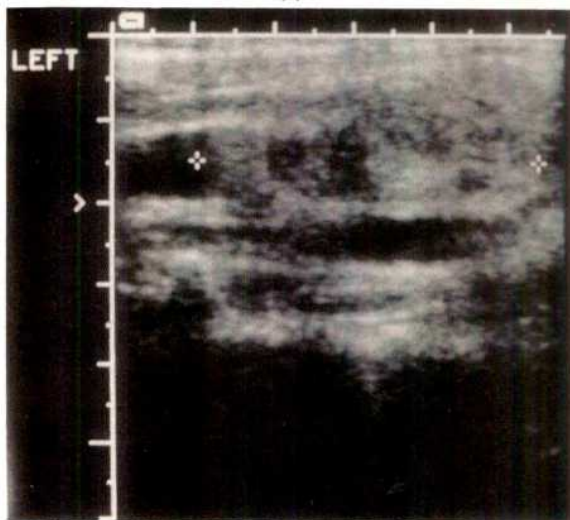
Figure 1. A frontal chest radiograph.

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What abnormalities are demonstrated on the chest radiograph and ultrasound? What is your diagnosis?



(a)



(b)

Figure 2. (a) and (b) Show ultrasound examination of the neck.

The chest radiograph revealed bilateral pleural effusions which were compatible with the hyperstimulation syndrome. Diagnosis of a pulmonary embolism was also made, but in view of the strong clinical evidence and early pregnancy an isotope ventilation/perfusion scan was not performed. The patient was heparinized for 7 days after which anticoagulation was discontinued.

The ultrasound examination revealed a markedly distended left internal jugular vein. The lumen was completely occluded by echogenic material. No Doppler signals were obtained distal to this mass. The other structures in the neck and the right internal jugular vein were normal. The appearance of the left internal jugular vein was consistent with thrombosis.

The appearances are those of a thrombosis of the left internal jugular vein. These thrombotic episodes are presumed to be caused by hypercoagulability secondary to ovarian hyperstimulation and pregnancy.

Discussion

Thrombosis of the internal jugular vein is relatively uncommon but is most frequently associated with central venous catheterization (Krepes et al, 1981; McNeill, 1981). The incidence is gradually rising with the increase in the use of catheters for intravenous feeding, venous pressure measurement, chemotherapy and rapid fluid administration. Spontaneous thrombosis is extremely rare but occasional cases (Witte & Lameris, 1986) have been reported. In these cases factors such as reduced blood flow (e.g. chronic heart failure) or hypercoagulability (e.g. oral contraceptives) may play a role. In this patient the hypercoagulability was associated with severe ovarian hyperstimulation, i.e. massive ovarian enlargement, ascites and pleural effusion (Painvain et al, 1987), secondary to her treatment for infertility. In the absence of recent venous catheterization the diagnosis is often not considered (Albertyn & Alcock, 1986) and a high degree of clinical suspicion is required in the presence of non-specific clinical findings. Other less frequent causes included contiguous head and neck infection (Yau & Norante, 1980) and intravenous drug abuse (Merhar et al, 1981).

The diagnosis can also be made using phlebography

(Chastre et al, 1982), scintigraphy (De Navdo & De Navdo, 1977), computed tomography (Albertyn & Alcock, 1986) and magnetic resonance (Braun et al, 1985). The advantage of ultrasound is that it provides a non-invasive, accurate method of establishing the diagnosis and may exclude other causes of neck swelling.

Doppler studies are valuable in demonstrating reduced or absent flow and are particularly helpful if there is a very recent thrombosis, since fresh clot has identical acoustic properties to liquid blood.

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Keywords: Jugular vein thrombosis, Ultrasound

Short communication

The use of a disposable nasoduodenal feeding tube for the small bowel enema examination

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Keywords: Small bowel enema, Nasoduodenal tube, Technique

The small bowel enema examination is a well accepted technique for the examination of the small bowel (Nolan & Cadman, 1987). Currently, the standard tubes used are the Nolan modification of the Bilbao-Dotter tube (Cook) and the Silk tube (Merck). We have been using a Levin-type nasoduodenal feeding tube manufactured by Vygon for jejunal intubation. This is a 125 cm long, 14F diameter tube designed for single use. It is easy and quick to pass and allows a fast barium flow rate. It is also cheap. We report a prospective randomized trial comparing the Vygon and Nolan tubes.

Patients and method

All patients undergoing a small bowel enema examination between February and October 1990 were considered for inclusion in the study. Those with a history of gastroduodenal surgery were excluded. The patients were randomized to two groups for intubation with either the Nolan or Vygon tube.

The intubation method was the same for both groups. The technique was developed from that used by our paediatricians for the passage of a Crosby capsule (Bisset, 1989). After anaesthetizing the pharynx with xylocaine spray the tube was passed with the patient supine, orally or nasally depending on the preference of the operator. When the tip of the tube reached the gastro-oesophageal junction, 50–75 ml of air were injected down the tube. A stiff guide wire was passed down the tube and the patient was turned to the right-side-down semi-prone position. The tube was advanced into the pylorus and the patient was then turned back to the right-side-down semi-supine position and the tube advanced into the distal duodenum or proximal jejunum keeping the tip of the guide wire in the pylorus. A 17% weight/volume of barium suspension was then infused and radiographs taken in the usual manner.

The screening and total times for each part of the procedure and any problems encountered during the examination were recorded. Small bowel distension was assessed by a radiologist without knowledge of the tube used for intubation. Patient acceptability was also assessed.

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Results

Forty-three patients were included in the study and intubation was successful in 37. Twenty patients were intubated with the Vygon tube and 17 with the Nolan tube. Age and sex distribution was similar for the two groups (Table I). The intubation and examination times are listed in Table II. There were no statistically significant differences between the times recorded in the two groups (independent *t*-test).

We were unable to intubate six patients, four with a Nolan tube and two with a Vygon tube. This was due to coiling of the tube in the fundus in three patients and failure to pass the pylorus in three patients. In two cases the alternative tube was tried without success. All but two of the failures occurred early in the study while two of the authors (R.A. and C.S.) were familiarizing themselves with the modified technique.

In one patient a Nolan tube could not be passed into the third part of the duodenum. A satisfactory examination was carried out with the tube in the second part of the duodenum with the patient semi-erect, although there was reflux of barium into the stomach.

Table I. Patient data

	Vygon	Nolan
Sex	8 male 12 female	6 male 11 female
Age (years)	46.7 (22–72)	51.1 (23–79)

Table II. Comparison of intubation, infusion and total examination times for the Vygon and Nolan tubes

Times (min)	Vygon	Nolan
Intubation		
Screening	3.5 (0.5–10)	3.2 (0.75–7)
Total	10.6 (2–17)	10.5 (5–15)
Infusion		
Screening	5.6 (2–9)	6.4 (3–10)
Total	13.1 (7–20)	14.9 (10–22)
Examination		
Screening	9.1 (3.5–18)	10.1 (3.75–16)
Total	25.2 (15–35)	26.2 (19–35)

Small bowel distension was excellent in 15 out of the 20 patients examined with the Vygon tube and in 10 of the 17 patients examined with the Nolan tube. Bowel distension was always adequate for diagnosis.

The examination was acceptable to the majority of patients. Eighty per cent of those intubated with the Vygon tube and 76% intubated with the Nolan tube said that they would have the examination again if necessary. Two patients examined with the Vygon tube had had previous small bowel enemas with the Nolan tube. Both found the Vygon tube more comfortable.

Discussion

The small bowel enema examination is considered to be the most sensitive method for detecting abnormalities within the small bowel (Maglinte et al, 1984).

The Vygon tube is a 14F tube, 125 cm long with four side holes. Eight, 10 and 12F gauges are also available; we use an 8F tube routinely for paediatric examinations. The tubes are flexible and we have found them easy to manipulate through the stomach. This allows a rapid intubation with short screening times. The calibre of the tube and the large side holes allow a fast flow rate of barium, which gave excellent bowel distension in 80% of our patients. It is possible for the guide wire to exit from one of the side holes if advanced too close to the tip of the tube whilst the distal part of the tube is curved. This is easy to recognize on fluoroscopy and we did not find it a problem. The tube is flexible and can be warmed prior to use for further softening if required.

Most reported series have used the Bilbao-Dotter tube or one of its modifications (Nolan & Cadman, 1987). This is a reusable tube but we have found it becomes rigid and difficult to manipulate with repeated use. Recently, the Silk tube has been introduced, and while some workers have found this a satisfactory tube (Nicholson et al, 1989), others have found problems in obtaining an adequate flow rate and have also described migration of the tube back into the stomach or tube kinking (Chippindale & Desai, 1989). We did not encounter problems of kinking with the Vygon tube. Migration of the tube back into the second part of the duodenum occurred in one patient but this did not prevent the examination being completed.

The tube is considerably cheaper than the Nolan or Silk

tubes, allowing it to be disposable. The current price of the Vygon tube is £0.77p compared with the Nolan tube which costs £14.15 and the Silk tube which is £14.00. The Silk tube is designed for single use only. The Nolan tube can be sterilized for re-use but we have found that it becomes more rigid and difficult to manipulate following repeated sterilization. We used the guide wire supplied with the Nolan tube for all our examinations, which can be autoclaved or kept in a suitable solution (such as Cidex) between examinations.

Some workers have been reluctant to adopt the small bowel enema procedure because of difficulty with intubation leading to long screening times (Ott et al, 1985). We found that with careful attention to technique, screening and examination times can be kept short. Our times are comparable to several other studies (Sanders & Ho, 1976; Nolan & Cadman, 1987; Nicholson et al, 1989).

We have found duodenal and jejunal intubation to be very easy with the Vygon nasoduodenal feeding tube. We would recommend its use for the small bowel enema examination.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Radiosensitization by 17 atmospheres pressure of air

The Editor—Sir,

As part of a study of the radiobiological effects of gas mixtures under ambient and hyperbaric conditions (Conere, 1989) we investigated the radiosensitivity of Chinese Hamster ovary (CHO) cells at 17 atmospheres pressure (1.7×10^6 Pa) of air. We found that such hyperbaric air caused a significant increase in radiosensitivity.

The cells were irradiated as a monolayer in 53 mm diameter Petri dishes seeded with 5×10^5 cells the previous day. Until the time of irradiation, the cells were incubated at 37°C in Gibco MEM growth medium with Hanks salts, 2 mM L-Glutamine, non-essential amino acids (0.6 mls/100 mls of medium), 15% foetal calf serum and 25 mM hepes buffer.

For the experiments the monolayers were washed in phosphate buffered saline (PBS) and then irradiated under 1 ml of PBS (with phenol red indicator) at, or close to, room temperature. Following the irradiation, the cells were trypsinized and suitable dilutions were plated in culture medium for growth into colonies.

The phenol red indicator in the PBS confirmed that no pH changes occurred, particularly during the pressurization schedules. An all-metal cylindrical tank with 4 mm steel walls was used. Pressure was increased at 0.1×10^6 Pa/min to 1.7×10^6 Pa, followed by a 15 min "soak time" at this pressure. The radiation dose was then given in less than 10 min at that pressure followed by decompression at 0.1×10^6 Pa/min. There was no significant difference in the plating efficiencies of the cells following exposure in PBS under normobaric and hyperbaric air conditions. Irradiations were performed using the parallel opposed dual head ^{60}Co unit, in the department of radiotherapy and oncology, St Thomas' Hospital, so that 1.74 Gy/min radiation dose was delivered to the cells in a "cross-fire" technique.

The data were fitted to dose-response curves using the linear quadratic survival curve model (Fig. 1). The two curves are significantly different (alpha values of 0.17 ± 0.05 and 0.25 ± 0.0007 Gy $^{-1}$ and beta values of 0.027 ± 0.0054 and 0.029 ± 0.0004 Gy $^{-2}$ for the normobaric and hyperbaric air data, respectively). The results indicate a radiosensitizing effect of hyperbaric air.

To our knowledge, there have been no previous reports of the effect of such a high pressure of air upon the radiosensitivity of mammalian cells, although Ebert and Howard (1957) reported a sizable radioprotective effect when 1.6×10^6 Pa of nitrogen was added to the ambient air environment of experimental bean roots.

Classical radiobiology indicates a slightly rising curve of relative radiosensitivity *versus* oxygen concentration under well oxygenated conditions. 1.7×10^6 Pa of air equates to 0.34×10^6 Pa of pure oxygen, at which level one might predict a 2% rise in radiosensitivity (assuming a K value of 9). Our data indicate an increase in radiosensitivity of about 16% at the 10% survival level related to the 17-fold increased oxygen concentration. The protective effect of nitrogen gas narcotic potency might also have been expected to increase with increasing nitrogen pressure. However, in these experiments oxygen seems to overtake nitrogen in the competition to occupy strategic sites within the cell.

Acknowledgments

We wish to acknowledge the helpful suggestions and comments of Dr O. C. A. Scott, The Richard Dimbleby Department at St

Thomas' Hospital, and thank Mr John Saunders and his staff from the Medical Physics Department for providing radiation dose calibrations. We also thank Professor W. S. Lowry, Department of Oncology, The Queen's University, Belfast, for his encouragement and the Ulster Cancer Foundation and Friends of Montgomery House for their financial support.

Yours etc.,

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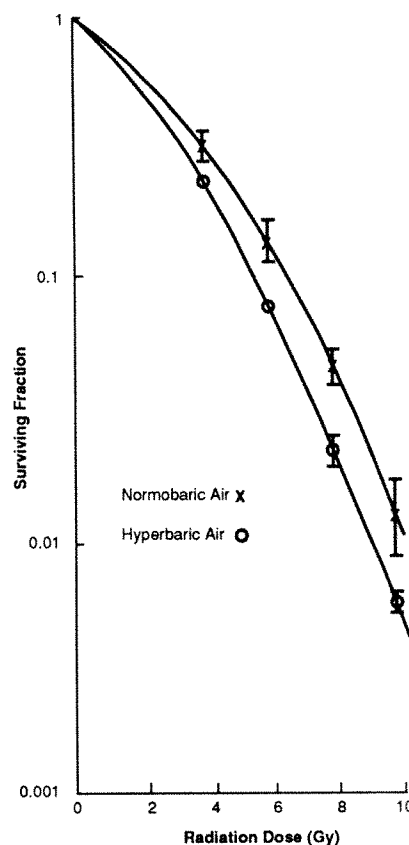


Figure 1. Dose-response curves for CHO cells irradiated with ^{60}Co gamma rays under different pressure conditions.

Dysphagia after fast neutron therapy to the head and neck

The Editor—Sir,

The letter from Duncan and Munro (1990) is very uncritical of the paper they refer to, "Dysphagia after fast neutron therapy to the head and neck", and gives a further false impression of the role of neutrons in radiotherapy.

The paper they referred to described a radiographic technique used by speech therapists at Hammersmith Hospital. The speech therapists had appealed to the radiotherapy and oncology department for patients with dysphagia to be tested so that the technique could be demonstrated. Nine patients who had had neutron therapy were referred and are described. Apparently no photon or surgically treated patients were tested, although dysphagia is well known following both; cancer itself causes dysphagia. There was no inclusion of the degree of pre-treatment dysphagia in the nine patients described although all neutron patients had late stage, infiltrating tumours and dysphagia was a common presenting symptom.

The paper omitted the stage of the tumours and the size of the radiation fields used, although the information was available in the notes. The paper makes an astonishing statement that "Dysphagia has previously gone unreported". Only one reference to neutron therapy at Hammersmith is given, but even in that dysphagia was discussed at length and numbers of patients affected were given.

The paper described a possibly useful technique but lacked objectivity and omitted relevant data. It reported, misleadingly, a "high incidence" of dysphagia in neutron patients. In fact more than 500 patients with head and neck cancer were treated with neutrons, so that nine is less than 2% — a very low incidence.

Yours etc.,

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DUNCAN, W. & MUNRO, A. J., 1990. Dysphagia after fast neutron therapy to head and neck. *British Journal of Radiology*, 63, 583.

Proceedings of the British Institute of Radiology

Radiobiology proffered papers (non topic)

Abstracts of papers presented at a BIR Radiobiology Sub Committee meeting held at 36 Portland Place, London W1N 4AT on Friday 22 February 1991

Chairman: R. S. Camplejohn

- The measurement of intracellular oxidative species induced by ionizing radiation using a flow-cytometric technique, by J. H. Peacock, C. M. Broughton, J. McNamara, M. G. Ormerod and J. C. Titley
- The optimum pressure of oxygen for radiotherapy, by P. M. Perry, J. J. Parker and A. H. W. Nias
- A comparison of the effects of the vasoactive agents flunarizine and hydralazine on transplantable and spontaneous mouse tumours: a ³¹P MRS study, by P. J. Wood, I. J. Stratford and G. E. Adams
- Therapeutic benefit with nicotinamide combined with carbogen or oxygen, by A. Rojas, E. Kjellen, M. C. Joiner, J. M. Collier and H. Johns
- Cardiac output and circulating blood volume in Wistar rats after local irradiation or intravenous adriamycin injection, by T. Kitahara and K. R. Trott
- Cellular recovery in primary human fibroblast cell lines, by N. G. Burnet, C. M. Broughton, J. J. Eady and J. H. Peacock
- Pulsed-field gel electrophoresis in the measurement of DNA double-strand breaks in human tumour cells, by S. J. Whitaker and T. J. McMillan
- Radiosensitization of melanoma cells, by N. Lemic-Stojcevic, A. H. W. Nias and K. Hellmann
- The effect of post-irradiation drug treatment on the chronic radiation ulcer of the large bowels in rats, by S. Tekieh
- The influence of epidermal cell migration and field contraction on the "chronic" radiation response of the rectum of the rat, by G.A. Ross and J. W. Hopewell
- Proliferative recovery in mouse skin and its dependence on irradiation schedule, by M. C. Joiner, H. Johns, A. Rojas, J. M. Collier and R. W. Tsang
- Accelerated and hyperfractionated radiotherapy with three daily fractions given during normal working hours, by C. H. MacMillan, J. Berridge, P. J. Bradley and D. A. L. Morgan

The measurement of intracellular oxidative species induced by ionizing radiation using a flow-cytometric technique

J. H. Peacock, C. M. Broughton, J. McNamara, M. G. Ormerod and J. C. Titley

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The "indirect effect" of ionizing radiation is believed to result from the production of oxidative species following the interaction of radiation with water.

Dichlorofluorescein diacetate (DCFH-DA) is a heterocyclic compound which reacts with hydrogen peroxide in solution. It has been used to measure the production of metabolic oxidative products in polymorphonuclear blood cells. DCFH-DA freely diffuses into cells, whereupon hydrolysis to DCFH occurs thereby trapping the molecule within the cell. Reaction with hydrogen peroxide produced in water by ionizing radiation leads to the quantitative production of the highly fluorescent dichlorofluorescein. Fluorescence can then be measured by flow cytometry. We describe the use of DCFH-DA to measure intracellular oxidative products in human tumour cells following ionizing radiation treatment.

In a total of seven human tumour cell lines, cellular fluorescence increased linearly with radiation dose over the range 0-20 Gy. Comparison of cells of differing sensitivity showed a similar relationship between fluorescence and radiation dose, suggesting similar levels of oxidative species production.

Following pre-incubation with BSO, which reduces intracellular GSH and is a scavenger of oxidative products, the level of fluorescence was increased by a factor of ~2 in all cell lines tested. In contrast, pre-treatment of cells with cysteamine dramatically reduced levels of fluorescence.

We believe that the use of DCFH-DA provides a simple method of measuring intracellular induction of oxidative species by ionizing radiation and may provide a powerful tool for investigating the "indirect effects" of radiation.

The optimum pressure of oxygen for radiotherapy

P. M. Perry, J. J. Parker and A. H. W. Nias

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The pioneers of the use of hyperbaric oxygen (HPO) in radiotherapy worked on the assumption that the higher the oxygen tension the more the oxygenation of hypoxic tumour cells. However, the maximum oxygen pressure that could be tolerated by the patients was 3 atm (unless anaesthesia was used) and this pressure has been used in nearly every clinical trial of HPO.

One physiological effect of HPO is vasoconstriction, however, this may be counter-productive. Anaesthesia may oppose this vasodynamic effect if used at the right time. We have investigated various schedules of anaesthesia and oxygen pressures used at different time intervals before irradiation of the C₃H mouse mammary tumour.

Our previous studies had shown that there is more regrowth delay after 25 Gy in tumours irradiated in mice breathing normobaric oxygen than in those breathing air, as might be expected. But, in both cases, this radiation response was reduced in anaesthetized animals in comparison with unanaesthetized control mice, when a time interval of only 10 min was allowed after anaesthesia. After 25 min, however, the response in air was back to the control level

and the oxygen group now showed significantly more radiosensitization.

We have found that when we use the 25 min time interval after anaesthesia with different pressures of oxygen, although there is even more regrowth delay with 2 atm pressure than 1, there is no further advantage from using 3 atm pressure of oxygen. 2 atm is clearly the optimal pressure to use in anaesthetized mice and there is even a small benefit from using this pressure in unanaesthetized animals.

(Supported by the Richard Dimbleby Cancer Fund)

A comparison of the effects of the vasoactive agents flunarizine and hydralazine on transplantable and spontaneous mouse tumours: a ^{31}P MRS study

P. J. Wood, I. J. Stratford and G. E. Adams

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The use of vasoactive agents to alter oxygenation in transplantable rodent tumours has been well documented. However, recent studies with spontaneous tumours in aged mice, or those arising in previously irradiated sites, suggest that manipulation of tumour physiology may not be as reproducible as results from transplantable murine tumours might predict.

Tumour response to physiological manipulation may be followed using ^{31}P magnetic resonance spectroscopy (MRS) and the present study uses this technique to monitor tumour response to the vasoactive agents hydralazine and flunarizine. The transplantable mouse tumours examined include SCCVII/Ha, KHT and 16C, and have been compared with spontaneous mouse tumours arising in the breeding stock of genetics division at the MRC Radiobiology Unit.

The transplantable tumours were intradermally situated on the backs of mice, 2 cm from the tail base. The mice were either anaesthetized with hypnorm/hypnovel, or unanaesthetized and restrained in jigs. The spontaneous tumours were situated at a number of sites and these mice were anaesthetized. Spectra were obtained using a 4.7 Tesla, 30 cm horizontal bore magnet, with a SISCO 200 spectrometer and a 7 mm diameter surface coil placed over the tumour. Each spectrum comprised 256 scans. Results are expressed as the ratio of the inorganic phosphate peak area to the total area of all peaks (Pi/total). Hydralazine increased Pi/total in all transplantable tumours studied, but had no effect on the spectra from spontaneous tumours, with one exception, where a small increase in the ratio was observed. In contrast, flunarizine reduced Pi/total in both the transplantable and spontaneous tumours.

These results indicate that spontaneous tumours in mice may provide useful information on modification of tumour physiology, more relevant to the clinical situation than that from transplantable tumour systems.

Therapeutic benefit with nicotinamide combined with carbogen or oxygen

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Enhancement of radiosensitivity with carbogen (95% O_2 + 5% CO_2) or oxygen combined with nicotinamide (the amide derivative

of vitamin B_3) was investigated in two rodent adenocarcinomas, mouse skin and kidneys, using a 10 fraction radiation schedule, and compared with the radiation response in air. Local tumour control, acute skin reactions, decreased renal ^{51}Cr -EDTA clearance and reduction in haematocrit were used as assays. Nicotinamide increased radiosensitivity of both tumours under all oxygen concentrations (21, 95 and 100% oxygen); carbogen plus nicotinamide gave the greatest increase. Relative to treatments in air without the drug, enhancement ratios (ER) at the TCD_{50} level were 1.17, 1.65 and 1.83 for CaNT tumours irradiated in air, oxygen or carbogen and 1.83 for CaRH tumours irradiated in carbogen plus the drug. In skin, radiosensitization was observed under all three gases, but was consistently less than that in tumours. ERs for renal damage were significantly lower than those in skin: $\text{ER}_{\text{kidney}}$ 1.07, 1.13 and 1.16 compared with ER_{skin} 1.08, 1.29, 1.38, for irradiations done in air, oxygen and carbogen plus nicotinamide, relative to air alone.

A therapeutic comparison was made by calculating the percent of locally controlled tumours with an X-ray dose sufficient to elicit a constant level of morbidity in skin and kidneys. Nicotinamide combined with carbogen increased the control rate of CaNT tumours from <2% in air alone to 67%, relative to skin, and from 0% in air to 95%, relative to renal damage; with oxygen the gain was slightly less (up to 46% local control, relative to skin, and 76% relative to kidney). The combination of carbogen/nicotinamide appears to be the most effective tumour radiosensitizer for use in clinical radiotherapy.

Cardiac output and circulating blood volume in Wistar rats after local irradiation or intravenous adriamycin injection

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Cardiac output and circulating blood volume were studied by determining the dilution of a bolus of $^{99}\text{Tc}^m$ using a gamma camera in male Wistar rats, locally irradiated with 20, 25 or 30 Gy of X ray to the heart, or given adriamycin intravenously at a dose of 1 mg/kg, 2 mg/kg or 3 mg/kg body weight. In irradiated rats, cardiac output decreased, with increase of radiation dose and increase of the interval after irradiation. Cardiac output was only 75% of control after 20 Gy and 49% after 30 Gy at 3 months.

Decrease in cardiac output and circulating blood volume were much faster after adriamycin injection. Cardiac output decreased to 67% of control after 1 mg/kg and 51% after 3 mg/kg at 2 weeks. Circulating blood volume decreased to 87% after 1 mg/kg and 75% after 3 mg/kg at 2 weeks.

Cellular recovery in primary human fibroblast cell lines

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Normal human fibroblasts show important radiobiological differences compared with cell lines derived from human tumours. Cell survival curves frequently demonstrate a true exponential shape. This contrasts with curvilinear dose responses observed for most tumour cell lines and also contrasts with clinical data on normal

tissue response which can be fitted to a Douglas-Fowler plot, implying a curvilinear dose response. Viewed simply, the lack of curvature of fibroblast cell survival curves suggests no capacity to accumulate sublethal damage and we might expect no effect of dose-rate or fractionation.

A number of primary fibroblast cultures were used to assess radiation response using clonogenic assays. Irradiation was given in single exposures at high dose-rate (HDR) of 1.1 Gy/min, in split doses at HDR and by continuous exposure at low dose-rate (LDR) of 0.01 Gy/min. In all 11 lines, response to single HDR irradiation was exponential with no shoulder. Do ranging from 1.05 to 1.65 Gy (SF2 0.15–0.30). In those cell lines in which split-dose experiments were carried out, little or no recovery was demonstrated.

At LDR most cell lines exhibited some recovery, *i.e.* decreased sensitivity, with exponential survival curves. However, the amount of recovery, which can be expressed as the ratio of LDR and HDR slopes, is seen to vary and this, consequently, alters the ranking of sensitivities. In one cell line no recovery was seen. This line had been established from a patient who developed severe acute reactions to a course of radiotherapy.

A spectrum of sensitivity of normal fibroblasts exists and this is well recognized. However, recovery, expressed as the ratio of LDR to HDR survival, may be as important in predicting clinically relevant sensitivity as "intrinsic sensitivity" measured by conventional HDR experiments.

Pulsed-field gel electrophoresis in the measurement of DNA double-strand breaks in human tumour cells

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Cells from the human bladder carcinoma cell line, RT-112, were irradiated under oxygen and hypoxia with and without misonidazole. Clonogenic cell survival assays demonstrated an oxygen enhancement ratio (OER) of 2, for a surviving fraction of 0.1 and 1.5 when all levels of survival were compared. A dose-modifying factor (DMF) of 1.9 was found for the addition of misonidazole to hypoxic cells. For assessment of DNA damage ^{14}C -thymidine labelled cells were encapsulated in low melting point agarose, irradiated with ^{60}Co γ -rays then lysed before CHEF-PFGE. Gels were electrophoresed for 4 days using a 60 min switch time at 45 V. When damage was assessed on PFGE as the fraction of total DNA mobile under electrophoresis (*i.e.* fraction extracted), an OER of 2.3 and DMF of 1.7 were found.

Gels were also sectioned after electrophoresis according to molecular weight and, from radioisotope counts of each section, an estimate of the number average molecular weight of the mobile DNA fragments was made. DNA dsb induction rates of 4.4, 1.2 and 2.1 were found for cells irradiated under oxic, hypoxic alone, and with misonidazole, respectively. Thus, an OER of 3.7 and a DMF of 1.5 for dsb induction were found. The discrepancy for OER found by this method, compared with the more simple method of fraction DNA extracted, may be caused by an underestimation (at doses <40 Gy) of dsb induction. In addition, it was found that when doses of oxic and hypoxic irradiation, which gave an equal fraction of total DNA extracted, were compared, the distribution of DNA fragments from cells irradiated under oxygen showed a smaller average fragment size. Whatever the mechanism of this finding,

we have demonstrated that simply measuring the fraction of total DNA extracted from irradiated cells may not be the best way of using PFGE to measure DNA dsb.

Radiosensitization of melanoma cells

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Richard Dimpleby Department of Cancer Research, UMDS, St Thomas' Hospital, London, SE1 7EH and *Radiotherapy and Oncology Department, Westminster Hospital, London, SW1P 2AP

Malignant melanoma is usually considered to be a radioresistant tumour, perhaps because the radiation survival curves of melanoma cells sometimes show a large shoulder. One solution will be to find a drug which will sensitize the cells to radiation by reducing the size of such a shoulder. We have investigated the effect of Razoxane and its isomers using B16 mouse melanoma cells in comparison with the mammary epithelial tumour line EMT6. Razoxane (ICRF 159) is a racemic compound whose optical isomers are known as ICRF-186 (L) and ICRF-187 (D).

The physical properties and the cytotoxicity of the D- and L-isomers are similar, but they differ in their radiosensitizing ability. Cell survival was determined by the clonogenic method and the sensitizer enhancement ratio (SER) was calculated at the 10% survival level. Increased sensitivity to X-radiation was observed in cells pre-treated for 24 h with 200 $\mu\text{g}/\text{ml}$ ICRF 159, 186 or 187. With EMT-6 cells the SER was 2.8 with 186, 2.1 with 187 and 1.9 with 159. However, with B16 F₁ mouse melanoma cells the SER was only 1.2 with 186, and with 159 and 187 it was 1.1. This was seen mainly as a reduced shoulder of the survival curve. However, this enhancement was obtained with drug doses which are toxic.

(Research supported by the David Price Melanoma Trust)

The effect of post-irradiation drug treatment on the chronic radiation ulcer of the large bowel in rats

S. Tekieh

Department of Radiation Biology, The Medical College of St Bartholomew's Hospital, Charterhouse Square, London, EC1M 6BQ

Groups of male Wistar rats were irradiated with single doses of 22, 24, and 26 Gy, respectively. A protein-free extract of calf blood known as ActoHorm was injected intraperitoneally on a daily basis during and after the acute phase following irradiation, or at a late stage when chronic ulceration was detected.

We were able to alter the clinical and histological picture of radiation induced late damage in the rectosigmoid of some animals. The results showed that ActoHorm has an effect on the severity and onset of the ulceration in the rat rectum, especially when the animals were treated from 3 weeks after irradiation onward. Treating the animals at the onset of ulceration delayed the progression of severity of the ulcers by 1–2 weeks as compared with controls.

Generally, the rectal ulcers in the treated animals were more superficial and smaller compared with the control animals. The microscopical presence of infiltrating epithelial cells in the submucosa and the formation of colitis *cystica profunda* suggests that stimulated regeneration has taken place.

The influence of epidermal cell migration and field contraction on the "chronic" radiation response of the rectum of the rat

G. A. Ross and J. W. Hopewell

CRC Normal Tissue Radiobiology Research Group, Research Institute, Churchill Hospital, Oxford OX3 7LJ

A simple model has been developed to assess radiation-induced damage to the rectum of the female Sprague Dawley rat. Two pelvic fields were used, one involved the irradiation of 30 mm of rectum and was based on the anal margin, whilst the other was 20 mm long and extended proximally from the distal edge of the vagina. The upper margin of both fields was the base of the bladder. Irradiations were with single doses of 250 kV X rays.

Following doses of ≥ 18.5 Gy, denudation of the rectal mucosa with oedema of the submucosa was observed within 7 days. By the fourteenth day, this lesion had progressed to mucosal sloughing with an increase in the degree of submucosal oedema. Although the initial reactions were identical for the two fields, the subsequent progression of the lesions was dependent on the field size. With the 20 mm long field, a deep circular radionecrotic ulcer developed rapidly and this ultimately caused the compression on the urethra against the symphysis pubis. The resultant amicturition caused animal morbidity within 30 days of irradiation. With the 30 mm long field, the migration of epidermal cells from around the anal margin had covered areas of a mucosal denudation. This stratified covering of an otherwise denuded area prevented the development of deep ulcerative lesions and, consequently, animals did not succumb from the secondary urethral complication. This was reflected in the significantly higher ($p < 0.001$) ED_{50} isoeffect dose for the urethral complication with the 30 mm (28.5 ± 0.7 Gy) compared with the 20 mm field (23.4 ± 0.5 Gy).

Using a quantitative dissecting microscope technique, the length of the irradiated rectum was found to contract significantly ($p < 0.01$) within the first 7 days of irradiation, irrespective of the initial field size: after 23 Gy the irradiated length was only 70% of its initial size. The degree of this early contraction increased with an increase in radiation dose. With the 30 mm field the continued reduction in length of the denuded region of rectum could be attributed to a significant progressive ingrowth by the epidermis from the anus. 4 weeks after 23 Gy this covered some 49% of the contracted field. After a dose of 35 Gy the sterilization of the epidermal cells around the anus prevented their migration into the rectum. Deep rectal ulceration occurred and resulted in a similar incidence of urethral complication for both field sizes (92%).

The migration of epidermal cells from the anus was, therefore, implicated as a major cause of the difference in the ED_{50} isoeffect dose for secondary urethral compression observed between the two fields.

Proliferative recovery in mouse skin and its dependence on irradiation schedule

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We have measured the proliferative recovery in the skin of WHT mice feet, during and after fractionated and single-dose X-ray

treatments. Repopulation of clonogenic epidermal stem cells was inferred from an increase in a top-up dose of neutrons needed to express acute skin reactions. No repopulation occurred before 12 days after treatment started, whatever the schedule of X-ray treatment given, even with single doses. This is, therefore, the minimum time required for this tissue to sense the damage before repopulation can be triggered. Irradiation with one 2 Gy dose per day allowed repopulation to commence during treatment given over 12–20 days. However, for 2×1.5 , 3×1.5 or 2×2 Gy per day given over 12–16 days, repopulation was not seen during treatment. This difference may reflect a dose threshold of 2–3 Gy per day needed to maintain a cell-cycle block. After completing these 2 or 3 fraction per day schedules ≥ 12 days, there was a further delay in the onset of repopulation of about 4 days. Single X-ray doses of 3 or 6 Gy given 12 days after a previous single dose, just before repopulation would otherwise begin, caused a delay in the onset of repopulation of about $1/3$ to $1/2$ per Gy. For all schedules tested, when repopulation commenced it was faster with increasing damage inflicted by the prior X-ray treatment. Longer overall treatment times also increased the rate of repopulation after it started. Clonogen doubling times were estimated as short as 16 h in the fastest examples.

Accelerated and hyperfractionated radiotherapy with three daily fractions given during normal working hours

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The resource implications for radiotherapy treatment given out of normal working hours are substantial. Accelerated, hyperfractionated radiotherapy is a tool to enable reduction of overall treatment time without excessive late damage, but may entail extended working hours for the radiotherapy department.

We have investigated the use of such a schedule of radiotherapy with 3 fractions given daily between 0830–1700, 5 days per week to treat Stage III and IV laryngeal carcinoma during the period 1983–1990. Initially, a split course regimen of 1.5 Gy per fraction was used, but this was modified because of toxicity. Since 1986, 26 patients have received fraction sizes of 1.1 Gy with an interval of 3–4 h between fractions during normal departmental working time, to a total dose of 60 Gy over 4 weeks. 22 of the 26 patients achieved control above the clavicles (including one with nodal relapse who was salvaged by radical neck dissection and one with local recurrence salvaged with laryngectomy); four patients died from uncontrolled locoregional cancer, and three from intercurrent disease whilst clinically free from tumour. Actuarial 3 year survival is 67%; disease free survival at 3 years is 80%.

Acute reactions were brisk but tolerated, and no severe late damage has been observed. Nine patients had the spinal cord included in the first phase of radiotherapy to a dose of 39.6 Gy in 36 fractions, so far without any evidence of late damage (median follow-up 23 months with four followed for >3 years).

Although numbers are small, the results from this pilot study may suggest that any benefit from accelerated and hyperfractionated radiotherapy could be obtained utilizing treatment delivered during normal departmental working hours.



BIR Bulletin

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The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Developing the public understanding of science

What is COPUS ?

Science and technology affect most aspects of daily life. Much industrial and public policy and many private decisions involve science and require informed public debate. But recent studies show that the public is largely uninformed about science, in spite of being interested in it.

One outcome of the Royal Society's Bodmer report was the foundation of COPUS in 1986 by the Royal Society, the British Association for the Advancement of Science and the Royal Institution. Membership is drawn from each of the founder institutions and from the media, museums, education, industry, Government and Parliament. COPUS provides a focus for a broad programme to improve public awareness of science and technology in the UK. Its activities are run by the three founder bodies. COPUS also acts as a central forum for organizations active in the public understanding of science, thus helping to maximize their use of limited available resources.

Scientists themselves can do the most to raise the public understanding of science. Much of this will be on an individual basis. COPUS is working in a number of ways to facilitate such activity and encourage networks of enthusiasts.

Using the influence of its founders, particularly the Royal Society in this instance, COPUS is pressing the case strongly with funding bodies that some contribution to the public understanding

of science should become a requirement for obtaining a science doctorate.

It is also busy developing a network of those concerned with promoting scientific public relations activities of learned and professional societies, research councils and higher education institutions, and the individuals who want to be involved. A series of guidance leaflets on promoting science for learned societies and professional associations is being developed that will cover topics such as how to convince members of the value of promoting science, how to run a press briefing, write a press release and react to press enquiries. COPUS intends

to help by sending staff and members of learned and professional bodies on specially designed courses on how to interact with the media.

Another important way in which COPUS is working to influence scientists themselves is the Media Fellowship Scheme, run by the British Association, which enables scientists and engineers to work for up to two months in the British media. The scheme aims to overcome scientists' suspicions of the media, to give them an insight into how the media works, and to improve their own communication skills. It is aimed at professional scientists and engineers working in higher educa-



The Floating Point Science Theatre uses mime, dance and audience participation to illustrate scientific mechanisms and engineering.

tion, industry, research organizations and the Civil Service. There have already been 28 fellows who have taken up placements in the news and features departments of national radio, television, science magazines and newspapers. Media fellows back in their institutions have continued in promoting public understanding of science by, for example, making promotional videos, freelance science writing, acting as a scientific adviser to an MP, and taking part in a BBC debate on the future of television and the role of science in broadcasting.

The Royal Society's Michael Faraday Award, a direct outcome of the Bodmer report, encourages scientists to regard public understanding of science as an essential and natural part of scientific life. It is made annually to the active scientist who has done most to promote in the UK the public understanding of science. COPUS recommends the recipient for the Award. Past winners of this Award are Professor Charles Taylor, Sir Peter Medawar, Professor Christopher Zeeman, Professor Colin Blakemore and Dr Richard Dawkins.

COPUS supports individual efforts to raise the public understanding of science too. Grants are available which are considered twice a year in March and in October. COPUS has already funded over 100 projects and this direct financial

support will continue and be extended to attract proposals from new sectors. All sorts of ventures have been supported including science workshops, scientific dance and theatre, scientific explanations in museums or other visitor attractions, public talks and demonstrations of scientific topics to non-scientific audiences and so on.

COPUS can only hope to encourage scientists to promote their subject more widely. It is up to the scientists to take up the challenge and work at imaginative ways of achieving this objective. COPUS aims to try and help those enthusiasts and to inspire others.

A number of other COPUS activities are aimed at the wider public:

The Science Book Prizes for adults' and childrens' popular science books.

Encouraging greater science coverage on television in drama, entertainment, news and current affairs, as well as in designated science programmes.

Working with museums, interactive science centres and leisure attractions to enhance their potential science components.

Science in Art featuring the way in which science and technology have influenced art.

The Westminster Fellowship Scheme to second professional scientists and engineers to work with Parliamentarians.

Suggesting speakers for the public lectures of its sponsoring bodies.

Collaboration with industry to improve the understanding of science of the industrial workforce.

Contact with the City to encourage recognition of the R & D function of a company in generating scientific and technological innovation to provide longer term financial survival and stability.

Discussions with women's groups about science awareness courses and with editors of women's magazines to encourage and support wider consideration of scientific issues.

Giving scientific seminars for Civil Servants.

COPUS has published a forward look of activities over the next five years, *COPUS Looks Forward*. This and other leaflets about COPUS are available from the *COPUS Executive Committee*, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG (Tel: 071-839 5561 ext. 266).

JILL A. NELSON
COPUS Executive Committee

Annual report of the BIR Hong Kong Branch for the year 1989/90

The Annual General Meeting 1989/90 was postponed to Friday, 8th March 1991. The delay was due to the difficulties in getting the speakers and the sponsorship, and more important, the movements of officers within the Committee.

We were able to hold two meetings during the year. The first meeting was on Tuesday, 5th June 1990. The speaker was Dr Martin Steiner, Consultant radiologist, Sheffield Children's Hospital, UK. He spoke on paediatrics including malrotation of the midgut, ultrasound in the acute abdomen, cystic lungs or problems in the older lungs.

The second meeting was on Friday, 8th March 1991. The speakers were Dr J.

Skucas, Consultant, Department of Diagnostic Radiology, Rochester General Hospital, New York, and Dr D. Carr-Locke, Director of Endoscopy and Clinical Gastroenterology and Associate Professor of Medicine, Harvard Medical School. The topic was "The role of glucagon in modern radiology and modern gastroenterology".

The BIR (Hong Kong Branch) was graced by a visit from Professor C. R. Hill, then BIR President, on the 16th May 1990. He was en route to Beijing for the International Congress on Medical Radiation Physics. Professor and Mrs Hill were met by our President Dr Winnie Ngai and the Secretary. Matters concern-

ing the general business of the Hong Kong Branch were discussed.

The election of the office bearers for the year 1990/91 is postponed to the AGM. Dr Lau Kam Ying, the Honorary Treasurer resigned and emigrated to Australia last August.

A number of radiologists and radiographers have resigned from membership and have emigrated to Australia and Canada during the year. It is anticipated that activities will pick up when the new officers have been elected.

ROBERT LEUNG
Honorary Secretary

Robert C. Tudway

Robert C. Tudway was born in Scotland in 1912, studied medicine at University College Hospital and trained as a radiotherapist at the Middlesex Hospital before becoming Consultant Radiotherapist-in-Charge of the Department in Bristol during the late forties. He retired in 1977 and died on 13 February 1991.

Bob, or "Tud" as he was known to his friends and colleagues, was a skilled and talented medical politician and under his leadership the Radiotherapy Department at the Bristol General Hospital soon became a major provincial centre, outgrowing its accommodation and extending beyond the basement which housed one of the earliest cobalt teletherapy units to be installed in a provincial centre.

In the 1960s there was some support for the development of purpose-built radiotherapy centres in major cities and, by virtue of his skilful lobbying, Robert Tudway was instrumental in obtaining the agreement of the Department of Health to build a new Centre in Bristol, on a site adjoining the Bristol Royal Infirmary.

At this point he was in his element, confounding architects with his attention to detail and, in hard hat and wellingtons, supervising the builders during construction.

The Centre was equipped with the first high energy betatron to be purchased by the National Health Service and is the largest and most comprehensively equipped cancer hospital in the South Western Region. As a tribute to his achievement, the building was designated "The Robert C. Tudway Building" on his retirement.

He excelled as a committee man both locally and nationally. In Bristol he chaired almost every conceivable committee and was a member of the Board of Governors of the United Bristol Hospitals. Nationally, he was President of the British Institute of Radiology from 1970-71, President of the Section of Radiology of the Royal Society of Medicine and on the Council of the Faculty of Radiologists, as well as an Examiner for the Fellowship.

His understanding of the need for basic sciences in radiotherapy was founded on his First Class Honours Degree in Physics awarded in 1944. Together with

Herbert Freundlich, who was Head of the Department of Medical Physics, he developed, during the late 1960s, one of the first computer-based radiotherapy planning systems in the UK. Later he was instrumental in the creation of a biophysics research floor within the Radiotherapy Centre. He also established the appointment of senior scientists to the Hospital Medical Committee with honorary consultant status.

A visitor to the Radiotherapy Centre would probably have found him leaning on the corridor wall, deep in quiet conversation, plotting no doubt, but always in the interests of his Department.

When Bob retired, a laithe was amongst the gifts that he received from his colleagues. He had always taken a keen interest in the Radiotherapy Workshop; evidently he also thought that it was a lot of fun.

He will be greatly missed by his wife Winifred and by their four sons, three of whom are doctors.

PROFESSOR PETER WELLS
DR HAROLD ECKERT
DR ALAN PREECE

Radiographers needed at the BIR

Whatever part you play in the world of radiology and the radiological sciences, you should know that you are eligible to join the British Institute of Radiology.

Radiographers play a vital role in radiology, helping to produce the medical images by one form of radiography or another, and therefore have an important part to play in the Institute's activities and meetings.

The history of the Institute, and its link with the College of Radiographers, is an interesting one. In 1897, in London, a meeting of medical men interested in the study of X-rays formed a society which

became known as the Röntgen Society. In 1927, this society became the British Institute of Radiology. In that same year, the College (at that time it was the Society) of Radiographers, became affiliated with the BIR. The College and the Institute shared the same premises at 32 Welbeck Street in London from 1927 until the College moved to 14 Upper Wimpole Street in 1968.

At the BIR all persons interested in radiation science and medical imaging are welcome, and eligible to join and take an active part in proceedings. There is no entrance examination. Upon receipt of a

completed application form, the radiographer member will receive the British Journal of Radiology monthly. He or she will be able to come to the meetings of the Institute and make use of the now enlarged and up-dated library at 36 Portland Place in London.

For any further information about the BIR, the benefits of membership or an application form to join the Institute please contact Mr Tony Hudson, Administration Manager.

MR GRAHAME MOUNTFORD
MBA, MCAM, DipM, MBIM, FCR

Product News

Siemens Mobile Clinic Helps in Armenia

A self-contained mobile diagnostic clinic sent to Armenia to help in the area devastated by the 1988 earthquake has recently completed six months of service. During this time the clinic has travelled over 750 km, visiting many remote areas throughout the Republic.

Siemens Medical Engineering was responsible for the supply of the clinic which is housed in a custom-built trailer designed and built by James Cocker & Sons (Stockport) Ltd. Facilities include: reception area, X-ray room, ultrasound room, darkroom and toilet. A 60kVA diesel-electric generator provides power for all the onboard electrical equipment including the X-ray machine. The mobile clinic was a gift to the people of Armenia from funds provided by the British Red Cross Society.

More than 2,500 patients have been treated to date. Cardiac and abdominal examinations are carried out using ultrasound, EKG, EEG and echo EEG, lung function, endoscopy and X-rays. Other British manufacturers who supplied equipment were Diagnostic Sonar (cardiac and general ultrasound machines), Knight X-ray Ltd (patient treatment couch), LEC Ltd (medical refrigerators) and South Midland Communications Ltd (telecommunications).

For more information contact David Sanders, Siemens plc, Medical Engineering, Siemens House, Windmill Road, Sunbury-on-Thames, Middx, TW16 7HS. Tel: 0932 75232

Correction

Our apologies are extended to Nycomed and to all those who have been trying to telephone them regarding their new product which was featured in the June Bulletin (B57).

Please note that for further information about Nycomed's AS200 — the new automatic injector for CT enhancement, please contact Linda Stuttard.

Tel: 021-742 2444

First European CT scanner for Veterinary Clinic

The Faculty of Veterinary Medicine in Utrecht (The Netherlands) have installed a Philips Tomoscan CX/S CT scanner for veterinary examinations. Professor Kees Dik, the head of the Faculty's radiology department, points out that the opening of the gantry of the CT scanner will never allow total body scans of horses or cows but the extremities, the legs or head, can be scanned without a problem. For the average dog or cat the scanner is suitable for whole body scans.

An extra large and wide patient table was made for big sized patients. Data such as the average size of a horse or cow were not standardly available and had to

be researched before design work could begin.

The new CT scanner enables the clinic to determine the severity of lesions in a much more precise way. Research is also being carried out on how to set up the protocols for the various veterinary examinations, for instance Professor Dik has found out that the best protocols for scanning a horse's head coincide with those of a human hip.

For more information contact Philips Medical Systems Press Office, PO Box 10, 000/5680 DA Best, The Netherlands. Tel: 31 40 762583



Preparing the horse for a head scan in the Philips Tomoscan

Breeze ventilators distributed by Kontron

The Newport Breeze, a ventilator designed specifically for neonatal and paediatric Intensive Care, is to be distributed by Kontron Instruments. The Breeze is the only ventilator to combine a pressure plateau ventilator with a volume ventilator, enabling it to deliver the accuracy needed for tiny neonates as well as the flow range required for older patients.

A special feature of the Breeze is its Duoflow system which separates the spontaneous flow system from the mechanical flow system for greater operational flexibility. The Duoflow system

incorporates an exclusive Intermittent Spontaneous Flow TM (ISF). This has several unique benefits including lower mean airway pressure, lower expiratory resistance and decreased work of breathing. The Breeze offers technology which is easy and clear to use with colour coded read-outs so that vital information can be read at a glance.

For more information please contact Kontron Instruments, Blackmoor Lane, Croxley Centre, Watford, Herts WD1 8XQ. Tel: 0923 50146

New 7-10 Minialarm from Mini-Instruments

The all-new 7-10 Minialarm is a mains operated installed radiation monitor with an audio/visual alarm that can be set to trip at any point on the scale. A range of compensated G-M probes give full-scale values from 75 μ Sv/h to 5 mSv/h whilst the 7-10 C, scaled in counts/s, can be used with most Mini-Instruments detectors including scintillation probes. Radiation intensity is displayed on an analogue meter scaled semi-logarithmically

which obviates range switching.

Other features include solid-state red and green lamps to show alarm status, latching/non-latching alarm, analogue output, remote alarm replay contacts and built-in test facility.

For further information contact Mini-Instruments Ltd, 8 Station Industrial Estate, Burnham on Crouch, Essex CM0 8RN. Tel: 0621 783282



New 7-10 Minialarm from Mini Instruments

Varian introduces linear accelerator for improved cancer treatments

The latest radiotherapy linear accelerator from Varian Medical Equipment is the Clinac 2300C/D featuring photon dose rates of 600 monitor units per minute (an increase of 50% over other accelerators), advanced software that allows special automatic beam shaping, and dual independent collimators which allow asymmetric field shaping. The first two features are required for delivering dynamic conformal therapy treatments.

For more information contact Christine Oliver, Varian Medical Equipment, Building 5B, 3045 Hanover Street, Palo Alto, CA 94304, USA. Tel: 415 424 5033

Toshiba introduces Small Parts Probe

A new probe from Toshiba can be connected to their alpha-series ultrasound systems SSA-270A, SSH-140A/G and SSA-250A. The small parts probe scans in black and white. The improved image quality, especially in the near field region enables the operator to observe detailed structures. The scope of diagnostic capabilities varies from the thyroid to female breasts and, most importantly, the shallow regions are now also accessible. The small parts probe will be available throughout Europe from autumn 1991.

For more information please contact Ms A Bromberg, PR department, Toshiba Medical Systems Europe bv, Schieweg 1, 2726 AN Delft, The Netherlands. Tel: 31 15 610121 Fax: 31 15 622359

Inventor of ultrasound imaging wins 1991 Japan Prize

Dr John J. Wild was recently awarded the prestigious \$375,000 Japan prize for his pioneering work in ultrasound. The awards are given by the Science and Technology Foundation of Japan to select members of the scientific community for achievements benefiting mankind.

Commenting on the award he stated his belief that ultrasound offers the best hope for accurate, early detection and diagnosis of small tumours of the breast and colon. He also voiced his concern that some modern equipment ignores tumour cellular structure. "Today's commercially available ultrasound machines do not have the sensitivity of the diagnostic equipment of the early 1950's. As a result, a great deal of tissue information is being technically thrown out...in an attempt to improve images, some equipment manufacturers have digitalized ultrasound equipment. While this reduces variables to numbers and the calculations that can be done with them, it cannot process "unseen" information from fine cellular structure...Until we get all the information available from the tissues themselves, we cannot afford to ignore data and continue to accept simple solutions to complex technical problems."

Dr Wild is currently working on a system to screen for small tumours quickly and automatically.

For more information contact International Public Relations Co. Ltd, 362 Park Avenue South (Suite 705), New York, NY 10010, USA. Tel: 212 213 3325

If you are interested in placing an article in the Product news section of the Bulletin please send all press releases to Helen Smith, Sales and Promotions Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT

Citramag from Bioglan

Citramag is a bowel evacuant for use in the preparation of the patient for all radiological examinations requiring a completely evacuated bowel. It may also be used prior to colorectal surgery. Citramag is presented in individual sachets containing 29.5 g. Just one sachet is dissolved in 200 ml of water and drunk.

For further information contact Bioglan Laboratories Ltd, 1 The Cam Centre, Wilbury Way, Hitchin, Hertfordshire, SG4 0TW. Tel: 0462 438444

Medical Interchange — An Innovative Enterprise

An interesting venture has recently been established by an Australian surgeon, Dick Crane, whose practice is in the Blue Mountains just to the west of Sydney. The organization is Medical Interchange and is designed to enable the exchange of practices between colleagues in Australia, New Zealand, the UK and Ireland. British radiologists may well be interested in this possibility.

Since returning to Australia from the UK about 8 years ago, Mr Crane has spent four to six weeks each year as a locum consultant surgeon in a major Sussex county hospital. "I have found that many colleagues have expressed an interest in being able to live and work for periods from three to twelve months in a totally different part of the world, yet one which has very similar professional standards," he says.

Immigration and registration requirements can be quite complex, but Medical Interchange will provide all necessary information to enable rapid compliance with these requirements," says Mr Crane. The scheme offers certain taxation and travel advantages as well.

Should you require more information about what Medical Interchange can offer, please do not hesitate to contact Mr Crane at 100 Lurline Street, Katoomba, New South Wales, 2780, Australia or by telephone or fax on (047) 82 3589.

New ultrasound system from IGE

The RT-x200, launched at a recent obstetrics and gynaecology meeting by IGE, features sector and linear array technology and has been designed to complement the successful RT2800. The new machine is highly manoeuvrable, enabling it to be used in a wide variety of examination situations, from neonatal surveillance at the bedside to operating theatres.

To ensure high image quality, the RT-x200 features a choice of grey curves with a wide dynamic range to allow adjustment for optimum image quality during an examination. Excellent spatial resolution is allowed through four electronic

focussing zones together with exceptional contrast resolution. The system has been designed to give the operator as much help as possible through simple adjustment and pre-programming of gain levels, greyscale and focussing zones backed up by automatic return to basic settings. Measurement and calculation software, pre or user-programmed obstetric tables and tabular display of values is standard on the system.

For further information contact Mike Head, Heads Public Relations, 2 Griffin Mall, Aylesbury, Buckinghamshire HP19 3BP. Tel: 0296 392460



BIR

Conferences Services

Is there a seminar, conference or evening get-together you want to organise, but you don't have the time? The BIR Conference Office may be able to help you. Please call Miss Vanesa Whitehead, Conference Manager, to discuss possibilities.

071-436 7807

Why not write for the BIR Bulletin?

The BIR Bulletin is an open forum for discussion for all those involved in the radiological sciences.

If you have an article that you would like published in the BIR Bulletin please send your material to the Honorary Editor, BIR Bulletin, The British Institute of Radiology, 36 Portland Place, London W1N 4AT.

New BIR Members

MEDICAL

Dr Javed AHMAD, MB, BS, FRCR, Dip (France), Diagnostic Radiologist
Dr John N. P. HIGGINS, MB, BS, MRCP, FRCR (London), Diagnostic Radiologist
Dr David HORTON, MB, BS (Hull, Humberside), Diagnostic Radiologist
Dr Kean T. TUNG, MA, MRCP, FRCR (London), Diagnostic Radiologist

NON-MEDICAL

Mr Colin J. FILDES, BA (Nottingham), Data-Med Computer Services Ltd
Mrs Sheila E. HEAP (Dunstable, Beds), Meadox (UK) Ltd
Dr Katharine S. HOLLAND, MA, D Phil (Little Chalfont, Bucks), Amersham International
Dr Richard A. LERSKI, BSc, PhD, FIPSM, MSRP (Dundee), Physicist
Mr David PIPER, HNC Applied Physics (Reading), Vertec Scientific Ltd
Ms Betsy RILEY, BA (London), American Medical Ltd
Dr Neil ROBERTS, BSc (Hons), MSc, PhD (Liverpool), Physicist
Mr Frans VERLAAN, HNC Electronics (Reading), Vertec Scientific Ltd

Library Update

The Systems Librarian is pleased to announce the completion of the automation and modernization of the Bernard Sunley library. The project has been completed within the planned timescale and budget.

Achievements

The following computerized services have been introduced:-

1. An Online Public Access Catalogue (OPAC) containing the BIR and COR bookstocks with a dedicated computer terminal for members use. This allows rapid and flexible access to the bookstock and also the production of printed subject catalogues and rading lists with ease.
2. Serials control of our 110 periodical titles including receipts and subscriptions control.
3. Online circulation system handling issue, return, reservation and overdue of material borrowed by members.
4. Ordering material for the library together with cost and fund accounting.
5. Installation of modem and Online searching software.
6. CD ROM installation.
7. Installation of DTP, WP and colour printer for promotional purposes, and designing library forms etc.
8. Setting up a media database to keep abreast of the latest developments in the field of radiology and related areas.
9. Setting up an organisations' database to keep track of both individuals and organizations in the field of radiology and related areas.
10. Setting up databases to cater for a wide variety of material ranging from audio visual to manuscripts, 3D archival objects and British Standards.
11. Establishing an inquiries log database to provide useful management information.
12. Setting up circulation lists of names and addresses to facilitate sending out promotional literature.

The tasks which are now being dealt with include advertising and promotion of the information service — which involves establishing a network of contacts and setting up a suitable scale of charges for the information service.

STEPHEN JOHNSON
Systems Librarian

Recent additions to the library

- BALL, J. & PRICE, T., 1989. Chesney's Radiographic Imaging.
- BARKOVICH, A. J., 1990. Contemporary Neuroimaging, Vol. 1. Paediatric Neuroimaging.
- DOBELBOWER, R. R. (Ed), 1990. Gastrointestinal Cancer: Radiation Therapy.
- DOBRANOWSKI, J. et al, 1990. Procedures in Gastrointestinal Radiology.
- EISENBERG, R. L. et al, 1990. Radiographic Positioning.
- ITURRALDE, M. P., 1990. Dictionary and Handbook of Nuclear Medicine and Clinical Imaging.
- MEDVEDEV, Z., 1990. The Legacy of Chernobyl.
- MINK, J. H. & DEUTSCH, L. (Eds), 1990. MRI of the Musculoskeletal System — A Teaching File.
- WEILL, F. S., 1989. Ultrasound of digestive diseases.
- ZERHOUNI, E. A. (Ed), 1989. CT and MRI of the Thorax.

The BIR Library is open week-days 9 a.m.-5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (excepting the historical collection) are available on loan.

BIR Calendar

Unless otherwise indicated, enquiries about these events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

MRI meeting

October 16, 1991

Organizer: Professor B. S. Worthington

Brachytherapy — The past, present and future

October 23 and 24, 1991

Institution of Electrical Engineers (Meeting to be held in association with Nucletron Ltd)

Organizer: Professor C. A. Joslin

Imaging of the oesophagus

November 5, 1991

Organizer: Dr A. Freeman

Hypoxic cell sensitizers: do they have a future?

November 15, 1991

Organizer: Dr R. Camplejohn

Ischaemic heart disease — limitations of non-invasive assessment

November 22, 1991

Royal London Hospital
Organizer: Dr N. Garvie

Vascular systems imaging

January 24, 1992

Organizer: Dr J. F. Reidy

Radiosensitivity

February 11, 1992

Joint BIR/RCR meeting
Organizer: Dr A. Gregor

Quality standards in nuclear medicine

February 18, 1992

Organizer: Dr A. Smith

3-D image analysis in medical imaging

February 25, 1992

Organizer: Professor M. A. Smith

Megavoltage portal imaging

April 9, 1992

Joint meeting with IPSM
Organizer: Dr W. Jones

Radiology & Oncology '92

18-20 May 1992

International Convention Centre, Birmingham

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

AEA Technology

Wigshaw Lane, Culcheth
WA3 4NE. Tel. 0925-252000 Ext. 4206
Product areas 7, 8.
Contact Mr J. G. Tyror, Director of Safety.

Agfa-Gevaert Ltd

27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Areas 1.
Contact Miss Anne Sparrow.

American Medical Ltd

PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC

Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr C. M. T. Medley, Sales and Marketing Manager.

Bard Ltd

Forest Houe, Brighton Road, Crawley,
West Sussex RH 11 9BP.
Tel. 0293 27888, ext. 2204.
Product area 2.
Contact Peter Dekkers, Product Manager.

British Nuclear Fuels plc

Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd

92 Uxbridge Road, Harrow, Middlesex,
HA3 6BZ. Tel. 081-954 2366.
Product areas 3, 6.
Contact Mr D. Lewis, Sales Manager.

Calumet Coach Co.

33 Shallbourne Rise, Camberley GU11
2EJ. Tel. 0276 64490.
Product areas: 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd

95A Finaghy Road, South Belfast
BT10 0BY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown, Managing Director.

Cea (UK) Ltd

25 Presley Way, Crownhill,
Milton Keynes MK8 0ES
Tel. 0908 263090. Fax: 0908 263546.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Clinical Press Ltd

Redland Green Farm, Redland, Bristol BS8
7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Data-Med Computer Services Ltd

10 Faraday Building, Highfields Science
Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fields, Sales Manager.

Du Pont (UK) Ltd

Wedgwood Way, Stevenage, Hertfordshire
SG1 4QN.
Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager,
Diagnostic Imaging.

E. G. & G. Limited

Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive
(Therapy).

Elscint (GB) Ltd

Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT.
Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing
Manager.

E-Z-EM Ltd

1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd

125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd

34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd

352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd

PO Box 66, Station Road, Hemel
Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
Product area 1, 3, 4, 6, 8, 9, 12, 13, 14, 15
Contact Mr J. J. G. Tweed, Manager,
Health Sciences Division.

Lanmark

PO Box 317, Beaconsfield, Bucks
HP9 2LR. Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC

3M House, Bracknell, PO Box 1,
Berks RG12 1JU. Tel. 0344 426726.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd

11 North Portway Close, Round Spinney,
Northampton NN3 4RQ. Tel. 0604-46132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M.A.S.MedicalLtd

Armtyage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Meadox (UK) Ltd

Matthew House, Matthew Street, Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and Marketing Manager.

Medical Xray Supplies Ltd

Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd

Travellers Lane, Hatfield, Herts AL10 8XB. Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and Marketing Manager.

Nuclear Associates

100 Voice Road, Carle Place, New York 11514-1593, USA. Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd

Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY. Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd

Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA. Tel. 021-742 2444.
Product areas 1, 3.
Contact Mr L. Birch Hansen, Managing Director.

Oxford Magnet Technology

Wharf Road, Eynsham, Oxford. Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems

Kelvin House, 63-75 Glenthorne Road, Hammersmith, London W6 0LJ. Tel. 081-741 1666.
Product areas 1, 2, 3, 4, 6, 9.
Contact Mr R. Van der Ploeg, Marketing Manager.

Premise Engineering Ltd

Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 0DR.
Tel. 09277-67433/63320.
Product area 8.
Contact Mr R. K. Beach, Director.

Quantel Ltd

Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA. Tel. 0444 232323.
Product areas 2, 10.
Contact Mr Christopher Trim, Publicity Officer.

Radiological Protection Services Ltd

61 Lind Road, Sutton, Surrey SM14 4PP. Tel. 081-643 6374.
Product area 8.
Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd

The Brow, Burgess Hill, West Sussex RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or Mr S. Hearne, Product Managers.

Siemens plc

Siemens House, Windmill Road, Sunbury on Thames, Middlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing Assistant.

Sony (UK) Ltd

Jays Close, Viabes, Basingstoke, Hants RG22 4SB. Tel. 0256 483564.
Product area 14.
Contact Richard Holt, Marketing Manager.

Toshiba Medical Systems UK

Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV

Schieweg 1, 2627 An Delft, The Netherlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P. Blonk, Office Manager, X-ray BU.

Vertec Scientific Ltd

5 Comet House, Calleva Park Estate, Aldermaston, Reading RG7 4QW. Contact Mr Frans Verlaan, Managing Director

Wardray Products Ltd

Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 0SP. Tel. 081-398 9911.
Product area 8.
Contact Mr R. B. Wardley, Managing Director.

William Cook (Eur) Ltd

6 Such Close, Letchworth, Hertfordshire SG6 1JF. Tel. 0462 482884 Fax: 0462 480944.
Product area 2.
Contact Tessa Phizacklea, Product Manager.

X-rite (H. Miller Graphics Ltd)

8 Moody Street, Congleton, Cheshire CW12 4AP. Tel. 0260 279988.
Product areas 1, 12.
Contact Mrs P. Dhanani, Medical Sales.

**KEY TO PRODUCT/
SERVICE AREAS**

- 1: Diagnostic X-ray including NMR and CT
- 2: Interventional radiology
- 3: Ultrasound
- 4: Nuclear medicine
- 5: Radiopharmaceuticals
- 6: Radiotherapy and oncology
- 7: Radiobiology
- 8: Radiation protection
- 9: PACS
- 10: Image processing
- 11: Nuclear fuel cycle services
- 12: Quality assurance.
13. Radiology data management computer systems
14. Video printing
15. Equipment leasing
16. Hospital-shared services
17. Medical Publishing

Meetings and Courses

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR

English for Doctors

August 12-30, 1991
Edinburgh, Scotland
Further details: Institute for Applied Language Studies, 21 Hill Place, Edinburgh, Scotland EH8 9DP.
Tel: 031 650 6183 Fax: 031 667 5927

The Bart's/London FRCR II Revision Course

August 27-29, 1991
London
Further details: Mrs C. Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholomew's Hospital, London EC1A 7BE.
Tel: 071-601 7531 Fax: 071-607 7024

6th World Congress in Ultrasound

September 1-6, 1991
Copenhagen, Denmark
Further details: Torben Larsen, Department of Gynecology, Herlev Hospital, DK-2730 Herlev, Denmark.

2nd International Workshop on Auger Spectroscopy and Electronic Structure

September 4-6, 1991
Lund, Sweden
Further details: Professor C. O. Almbladh, Department of Theoretical Physics, Lund University, Solvegatan 14A, S-22362 Lund, Sweden.

International Conference on Thoracic Oncology & Brachytherapy

September 12-13, 1991
New York, USA
Further details: Dr D. Nori, Booth Memorial Medical Center, Department of Radiation Oncology, 56-45 Main Street, Flushing, NY 11355, USA.

Fundamental Basis: Do Breast Microcalcifications have a specific Ultra-Structure?

October 9, 1991
France
Further details: M. J. Rodiere, Institut D'Imagerie Medicale, Miniparc - Bat 2, Rue de la Croix Verte, 34090 Montpellier, France.

Computed Body Tomography for the Technologist — State of the Art

November 7-10, 1991
Orlando, Florida
Further details: Programme Coordinator, The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner 20, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: (301) 955-2959

Implication of the New ICRP Recommendations on Radiological Protection Practices.

November 26-29, 1991
Salamanca, Spain
Further details: Commission of the European Communities, DG X11/D3, Rue de la Loi 200, B-1049, Brussels.

BMUS 23rd Annual Scientific Meeting and Ultrasound Equipment Exhibition

December 10-12, 1991
Bournemouth
Further details: The General Secretary, BMUS, 36 Portland Place, London, W1N 3DG.
Tel: 071-636 3714 Fax: 071-323 2175

6th Asian Oceanian Congress of Radiology

December 14-18, 1991
New Delhi, India
Further details: M. L. Malhotra, Executive Secretary, Aggarwal Imaging Research Centre, 10-B, Kasturba Gandhi Marg, New Delhi-110 001, India.

Non-ionising Radiation Protection

January 14, 1992
London
Further details: Dr D. N. S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Otlands Park, Linlithgow, West Lothian EH49 6AS. Tel: 031-244 2779

Skeletal Radiology Group of the Royal College of Radiologists

March 5-6, 1992
Coventry
Further details: Dr J. Chandy, Consultant Radiologist, X-ray Department, Coventry & Warwickshire Hospital, Stoney Stanton Road, Coventry, CV1 4FH. Tel: 0203 224055

International Symposium on Recent Advances in Diagnostic Imaging and Radiation Oncology

March 24-27, 1992
Kathmandu, Nepal

Further details: Dr Naresh Prasad, Department of Radiology, Baylor College of Medicine, Houston, Texas 77030, USA.
Tel: (713) 798 4415 Fax: (713) 798 5556

The Cambridge Meeting on Chest Disease

March 25-27, 1992
Cambridge
Further details: Dr C. D. R. Flower, Department of Diagnostic Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ. Tel: 0223 216203

6th Symposium Mammographicum

April, 1-3, 1992
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG.
Tel: 071-636 4430 Fax: 071-323 3100

Eurodop '92: Major International Symposium on the Medical Applications of the Doppler Effect in Diagnostic Ultrasound

April 5-8, 1992
Brighton
Further details: Eurodop '92, Bell Howe Conferences, 1 Willoughby Street, Beeston, Nottingham NG9 2LT.
Tel: 0602 436323

Progress of Radiation Protection

May, 1992
Essen, Germany
Further details: Professor Dr C.H. R. Reiners, Klinik und Poliklinik für Nuklearmedizin der Universität-GHS-Essen, Hufelandstr. 55, D-4300 Essen 1.
Tel: 02 01/7/23-20 32.

Eighth International Congress of IRPA

May 17-22, 1992
Montreal, Canada
Further details: IRPA8, 2155 Guy Street, Suite 820, Montreal, Quebec, Canada, H3H 2R9. Fax: (514) 932-9419

Third European Symposium on Uroradiology Imaging and Intervention

August 24-27, 1992
Denmark
Further details: Henrik S. Thomsen, Department of Diagnostic Radiology 54E2, Herlev Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark.
Tel: 45 44 53 53 00, ext. 278
Deadline for abstracts: March 1 1992.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

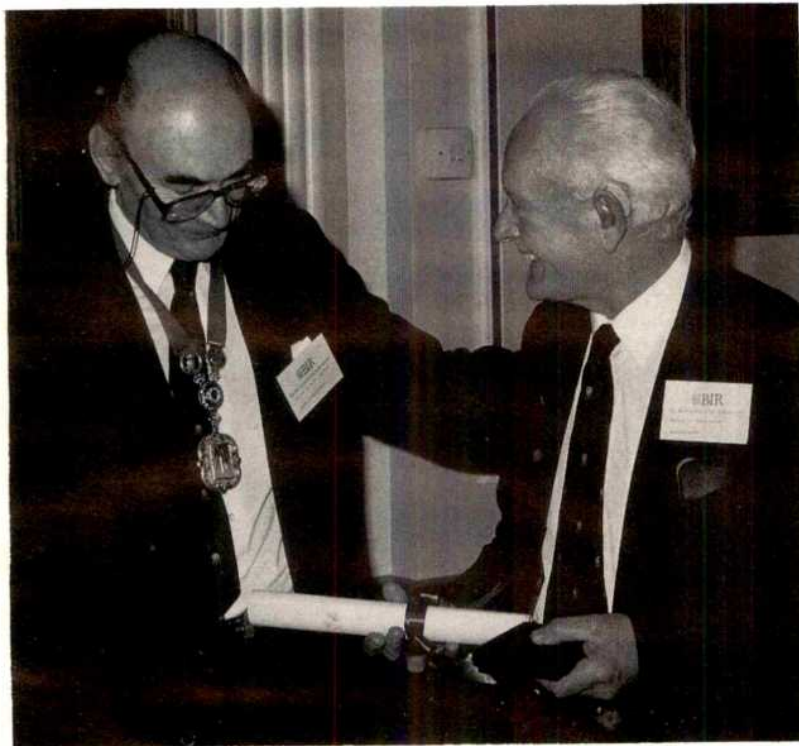


BIR Bulletin

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36 Portland Place, London W1N 4AT
The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

BIR Conversazione

Professor J. R. Mallard receives the Barclay Medal



Professor Charles Joslin shares a joke with Professor John Mallard while presenting the Barclay Medal to him.

John Mallard is one of the small band of outstanding figures who have won and maintained the high international standing of British medical physics. His scientific reputation has been built on a remarkable record of publications, including no less than twenty-three papers (several of them classics) in BJR.

Following a PhD at Nottingham, with a thesis on Magnetic Properties of Uranium-Iron Alloys, and a brief spell at the then Liverpool Radium Institute, he moved to Hammersmith Hospital as its first radioisotope physicist, later becoming Deputy Director of Medical Physics. This was a highly productive period when

he achieved a number of firsts in nuclear medicine and when, in particular, he pioneered clinical *in vivo* radioisotope scanning, along with Belcher and Mayneord in the UK and Cassen in USA, building the first UK clinical radioisotope scanner. Subsequently, following the work of Anger in USA, he built the first British gamma camera.

After a short period as Reader in Biophysics at St. Thomas, he was appointed in 1965 to the newly created Chair of Medical Physics at Aberdeen. In his inaugural lecture there he set out a number of goals, including the purchase of a cyclotron for therapy and PET imaging, developing electron spin resonance techniques for clinical imaging, and the introduction of an MSc course in medical physics.

Once settled into Aberdeen, he completed the radioisotope imager hat-trick, started at Hammersmith, by building one of the first radionuclide tomographic scanners, thus introducing computed tomography into nuclear medicine, somewhat before its advent in radiology.

It is said by his colleagues that, when his time comes, John Mallard's epitaph will read "He never knowingly threw out old equipment". He is also reluctant to discard good ideas: it was from a slight mutation of his interest in ESR that he developed the work of the Aberdeen team (initially with Jim and Meg Hutchison) in the science and practice of clinical NMR imaging. Big oaks from little acorns grow: in 1974 their subject was a dead mouse

(wee, sleekit, cow'rin', tim'rous beastie) but by 1980 they had become one of the first groups to be scanning patients, with their unique design of low-field, low cost imager, and were also doing pioneering work on the scientific basis of the subject. Despite the harsh economic climate he still continues to support new ideas in medical imaging. His current favourite is PEDRI (Proton Electron Double Resonance Imaging), with its aim to image free radicals in vivo. The idea, John insists, originates from a paper he wrote for Nature in 1963.

Developing medical imaging is not the only love of John's professional life: he always felt that there was a need for

graduates to be taught the practicalities of applying their basic scientific knowledge to medical problems. Thus, in 1968, he started up what has become one of the major courses in medical physics: a course whose graduates are now widely represented in other departments both in the UK and abroad.

John Mallard has an international view of science and, for the past thirty years, has been active in what has become the international organization of medical physics, of which he was founder Secretary-General and later President. His campaigning efforts to break the perceived division between medical physics and bio-engineering subsequently led him

to become the founder President of the International Union of Physical and Engineering Sciences in Medicine. He has also been the recipient of a number of major British and international honours and awards.

It would not be an exaggeration to say that John Mallard is a visionary in the world of medical imaging. But his success is due not simply to vision and inspiration (nor a touch of Aberdonian frugality); visitors to his office will notice on the bookcase behind him a sign "nil carborundum illegitimus" a fitting message for all scientists in today's harsh world.

P. F. SHARP

P. P. DENDY

Barclay Prize awarded to Professor I. Isherwood and Team

Ian Isherwood has been a Consultant Radiologist since 1961 and was appointed as the first Professor of Radiology in the University of Manchester in 1975. Since then the Department has become the largest training scheme in the UK with 50 postgraduate radiologists in training. He was responsible for the first CT brain scanner in operation at the Manchester Royal Infirmary in 1972, the first general purpose CT body scanner in Europe in 1975, and was involved with the early development of MR scanning from 1983. He has contributed to over 200 scientific papers and chapters in the field of diagnostic imaging, with special emphasis on physical aspects and clinical series. In his early publications, those on intrasosseous venography and air meatography were particularly noteworthy. He was associated with the first application of quantitative CT to bone mass measurement, published in the *Lancet* in 1976, and this has continued to be an important research interest in the Department. The significant advances made in his Department in the basic physics in CT and MR imaging have led to other areas of interest including tissue characterization and observer error. He has also applied conventional radiography and more modern imaging techniques to the examination of Egyptian Mummies, the reports of which make fascinating reading.

His achievements in scientific research and postgraduate education have been recognized both nationally and in-

ternationally. Ian is Radiological Adviser to the Chief Medical Officer at the Department of Health, a Commissioner to the International Commission of Radiological Units (ICRU), and President of the European Association of Radiology. His exceptional skills as a communicator and teacher have gained him an international reputation and he is much in demand as a speaker at home and abroad. Many honours have been bestowed on him from European radiological societies and he was awarded an Honorary

Doctorate of Medicine from the University of Zaragoza in Spain. His period as President of the British Institute of Radiology in 1984-85 was distinguished by a rejuvenation of the Annual Congress which now continues as the major national radiological meeting.

The award of the Barclay Prize is welcomed as a fitting recognition of the contribution made to radiological science by Professor Isherwood and by his leadership of his team.

J. G. B. RUSSELL



Professor Charles Joslin presenting the award to Professor Ian Isherwood

Röntgen Prize awarded to Dr T. Wheldon

This year's Röntgen Prize is awarded to Dr Tom Wheldon for his many excellent contributions to the Journal which have spanned a period of more than 15 years.

Tom Wheldon was originally a graduate of the University of Strathclyde where he obtained a degree in Physics in 1968. From there he moved to Glasgow where, apart from a short period in London at the MRC Cyclotron Unit (1979-1983), his work in radiation biology as applied to radiotherapy has gained him a well earned international reputation for excellence.

In his early years at Glasgow, Dr Wheldon was a student of the late Dr Jim Kirk where he developed his interest in the use of mathematical models in radiobiology and radiotherapy, and in 1973 he obtained a PhD at the University of Glasgow. This interest in mathematical models is a theme that has marked his success as a scientist in his career to date.

There are many aspects of his publication one could note but those that relate to the predictive modelling of normal tissue responses on the basis of a differing proliferation organization are perhaps the most widely known. However, in addition he has produced a series of excellent review articles on the use of mathematical models in experimental and clinical oncology, including a book on that topic published in 1988.

Dr Wheldon has for a long time served as an active member of the Department of Health Committee on Medical Aspects of Radiation in the Environment (COMMARE) and has been a contributing author to a number of their reports, particularly those relating to the possible increased incidence of leukaemia and other cancers in children or young people in the vicinity of nuclear installations. The area of research presently being pursued by Dr Wheldon and his collabo-

rators in Glasgow is the evaluation of means of increasing the selective delivery of anti-cancer therapy, with a special interest in the selective targeting of radionuclides in the treatment of neuroblastoma. This is an especially interesting and challenging approach which draws on his considerable experience as a physicist, mathematical modeller and experimental radiobiologist.

It has been a privilege to outline some of Tom Wheldon's most notable achievements, some of which have had a significant impact on my own research. The British Institute of Radiology has made a good choice in awarding him this year's Röntgen Prize.

J. W. HOPEWELL

*Dr Tom Wheldon was unable to attend the *Conversazione* but he will be receiving his prize in due course.*

Half an eye on the sky

"Red sky at night, shepherd's delight" must have a particular resonance for Sir Stephen Furness, a farmer who is also a landscape painter. Farmers have to get up early; artists and photographers should do so in order to capture that special ambience of the dawn light. Sir Stephen began his fascinating exploration of the ongoing attempts by artists to reproduce the "magic moment" in landscape painting by showing a slide of his farm in a golden misty dawn - the use of another part of the electromagnetic spectrum!

He went on to show how artists were influenced by the work of their contemporaries, including a river scene by Thomas Girtin of whom Turner said "had he lived, I would have starved".

Sir Stephen showed examples of work by Gainsborough and Constable, urging his audience to visit the current exhibition of the latter at the Tate, and explained the lengths to which artists went in order to work outside. A story about a lady artist returning to find that the cows had licked her painting clean may be apocryphal! Working outside quickly is essential as the light alters

dramatically during a couple of hours. He also pointed out how the quality of light in this country alone varies from the hard, diamond-bright light of the St Ives' beaches to the soft grey tones of the Lake District. Occasionally he slipped in one of his own paintings, commenting that he completed a particularly delightful view of an English meadow in high summer in an afternoon.

He showed slides illustrating the chiaroscuro light and shadow effect which lends drama and an operatic quality to paintings. The slides were not in chronological order as Sir Stephen explained that different schools were working simultaneously, but it included some modern paintings including a depiction of windsurfers in Cornwall where the artist had successfully captured the bright colours and frothy waves.

Sir Stephen was thanked by the President, Professor Joslin, who pointed out that the first question he was asked when inviting his speaker was the date of the event. If it had clashed with the lambing season, he said, we would have been out of luck.



Sir Stephen Furness

On a very wet and windy night in London the Painters Hall provided a welcome refuge with an excellent buffet being served after the lecture. This also gave guests an opportunity to talk further with Sir Stephen and make new acquaintances.

HELEN D SMITH

Library News

Current Journals Held in the Library

- ACR Bulletin
 ASTRO Newsletter
 Acta Oncologica
 Acta Radiologica
 Activity
 American Journal of Neuroradiology
 American Journal of Roentgenology
 Annales de Radiologie
 Annals of Nuclear Medicine
 Annals of the ICRP
 Applied Health Physics Abstracts and Notes
 Applied Radiation and Isotopes
 Archives of Radiology and Electrotherapy
 Archives of Skiagraphy
 Archives of the Roentgen ray
 Australasian Radiology
 BMUS Bulletin
 BSI News
 British Institute of Radiology Bulletin
 British Journal of Actinotherapy and Physiotherapy
 British Journal of Cancer
 British Medical Journal
 Bulletin of the International Union against Cancer
 Bulletin Officiel de la Societe Francaise
 Bulletins et memoires de la Societe de Radiologie Medical de France
 Canadian Journal of Radiography, Radiotherapy and Nucleography
 Canadian Nuclear Technology
 Cancer Research
 Cancer Treatment Reviews
 Cancer
 Cardiovascular and Interventional Radiology
 Cathode Press
 Cell Proliferation
 Chinese Journal of Nuclear Medicine
 Chinese Journal of Radiology
 Clinical Radiology
 Clinical Imaging
 Clinical Nuclear Medicine
 Clinical Oncology
 Clinical Physics and Physiological Measurement
 Computerised Medical Imaging and Graphics
 Computerised Radiology
 Computerised Tomography
 Critical Reviews in Diagnostic Imaging
 Current Contents (Life Sciences)
 Current Opinion in Radiology
 Current Opinions in Cardiology
 Current Opinions in Gastroenterology
 Current Problems in Diagnostic Radiology
 Dental Radiography and Photography
 Deutsche Rontgengesellschaft Informationen
 Diagnostic Imaging
 Diagnostica per Immagini
 Documents of the NRPB
 Egyptian Journal of Radiology and Nuclear Medicine
 Euro Specta
 European Journal of Cancer
 European Journal of Nuclear Medicine
 European Journal of Radiology
 European Journal of Surgical Oncology
 European Medical Ultrasonics
 Excerpta Medica. 14 Radiology
 Excerpta Medica. 23 Nuclear Medicine
 Gamma
 Gastrointestinal Radiology; a Journal of Abdominal Imaging
 HPA Bulletin
 Health Physics. The Radiation Protection Journal
 Hospimedica
 IAEA Newsbriefs
 IAEA News Features
 IAEA News
 ISR Newsletter
 ISRRRT Newsletter
 Index of European Radiological Journals
 Indian Journal of Radiology and Imaging
 International Atomic Energy Agency Bulletin
 International Journal of Hyperthermia
 International Journal of Applied Radiation and Isotopes
 International Journal of Nuclear Medicine and Biology
 International Journal of Radiation Biology
 International Journal of Radiation Oncology, Biology and Physics
 Investigative Radiology
 Japanese Journal of Nuclear Medicine
 Journal Belge de Radiologie
 Journal de Radiologie et D'Electrologie
 Journal de Radiologie, Radiophysique and Radiobiologie
 Journal of Nuclear Medicine
 Journal of Ultrasound in Medicine
 Journal of Clinical Oncology
 Journal of Computed Tomography
 Journal of Computed Assisted Tomography
 Journal of Interventional Radiology
 Journal of Medical Imaging
 Journal of Physical Therapeutics Quarterly
 Journal of Radiological Protection
 Journal of the Canadian Association of Radiologists
 Journal of the National Cancer Institute
 Journal of the Royal Society of Medicine
 Journal of the College of Australian Radiologists
 Journal of Thoracic Imaging
 Journal of X-ray Technology
 La Radiologia Medica
 Lancet
 Le Radium
 Library Committee Agenda
 Library Committee Minutes
 Magnetic Resonance in Medicine
 Medical Electrology in Medicine
 Medical Physics
 Medical Radiography and Photography
 Medicamundi
 Meditsinskaya Radiologiya
 Neuroradiology; a Journal Devoted to Neuroimaging and Interventional Radiology
 Nuclear Medicine and Biology
 Nuclear Medicine Communications
 Oncologia si Radiologia
 Pediatric Radiology
 Physical Therapeutics
 Physics in Medicine and Biology
 Proceeding of the College of Radiologists in Australia
 Proceedings of the American Society of Clinical Oncology
 Proceedings of the American Association for Cancer Research
 Proceedings of the Royal Society of Medicine
 Radiation Protection Dosimetry
 Radiation Research
 Radiatsionnaya Biologiya
 Radiographics
 Radiography
 Radiography Today
 Radiologia

Radiologia Brasileira
 Radiologia y Medicina Nuclear
 Radiologica Cancerologica
 Radiological Clinics of North America
 Radiologica Medica
 Radiological Protection Bulletin
 Radiology
 Radiology Now
 Radiotherapy and Oncology
 Rad
 Rays; International Journal of
 Radiological Sciences
 Revista Argentina de Radiologia
 Revista Brasileira de Radiologia
 Revista Italiana di Radiologia Clinica
 Revista Mexicana de Radiologia
 Revista de Biologia y Medicina
 Nuclear
 Revista di Radiologia

RöFo (Germany)
 Röntgen-Praxis
 Seminars in Roentgenology
 Seminars in Interventional Radiology
 Seminars in Nuclear Medicine
 Seminars in Ultrasound, CT and MR
 Skeletal Radiology
 Strahlenschutz in Forschung und Praxis
 Strahlentherapie und Onkologie
 Transactions of the American Roentgen
 Ray Society
 Ultrasonics
 Ultrasound in Medicine and Biology
 Urologic Radiology
 World Health
 X-ray Focus
 Zentralblatt für die Gesamte Radiologie
 Zentralblatt für Röntgenstrahlung,
 Radium und Verwandte Gebiete

BIR Calendar

Unless otherwise indicated, enquiries about these events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

MRI meeting

October 16, 1991

Organizer: Professor B. S. Worthington

Brachytherapy — The past, present and future

October 23 and 24, 1991

Institution of Electrical Engineers
 (Meeting to be held in association with Nucletron Ltd)
 Organizer: Professor C. A. Joslin

Imaging of the oesophagus

November 5, 1991

Organizer: Dr A. Freeman

Hypoxic cell sensitizers: do they have a future?

November 15, 1991

Organizer: Dr R. Camplejohn

Ischaemic heart disease — limitations of non-invasive assessment

November 22, 1991

Royal London Hospital
 Organizer: Dr N. Garvie

Vascular systems imaging

January 24, 1992

Organizer: Dr J. F. Reidy

Radiosensitivity

February 11, 1992

Joint BIR/RCR meeting
 Organizer: Dr A. Gregor

Quality standards in nuclear medicine

February 18, 1992

Organizer: Dr A. Smith

3-D image analysis in medical imaging

February 25, 1992

Organizer: Professor M. A. Smith

Megavoltage portal imaging

April 9, 1992

Joint meeting with IPSM
 Organizer: Dr W. Jones

Radiology & Oncology '92

18-20 May 1992

International Convention Centre,
 Birmingham

Radiology Information Centre Now On-Line

The launch of the newly automated Library and Information Service housed in the Bernard Sunley Library was marked by a reception held at the BIR on 17th June for sponsors Nucletron, BNFL/AEA, BMUS, the College of Radiographers, the Bernard Sunley Foundation and other organizations interested in the British Radiological Library Scheme (BRLS). The launch party was well attended with much interest being shown in the new library computer technology. Inaugural speeches were given by Professor Charles Joslin, the President of the BIR and Dr J. Reidy, Chairman of the Library Committee. Demonstrations of the new technology were given by Nigel Pegg of Pyramid Computers and Stephen Johnson, Systems Librarian for the BIR and architect of the automation project.

The aim of the BRLS project is to improve access to radiological information across the UK, providing a postal, fax and telephone enquiry service to the UK, Europe and beyond. The library databases will cover all aspects of radiological information from books and journals to information on areas such as radiological events and meetings worldwide, new products arriving on the market, research being carried out, services provided by NHS hospitals etc.

The Service is open to all those who have an need for information in any area of radiology including radiotherapy and

oncology, ultrasound, radiography, nuclear medicine, CT, NMR, radiation physics, radiation protection, radiobiology and the history of the development of these technologies. The BIR, as the oldest radiological society in the world, has a unique and comprehensive collection of materials and since June '91 a database on radiology which will dramatically improve access to this information. The BIR Library Scheme aims to have "all you need to know about radiology under one roof". If you work in the radiology field or are employed by one of the companies manufacturing the equipment used in this area of healthcare, can you afford not to contact us?

For further information contact: Stephen Johnson, Tel: 071 580 4085. Fax: 071 255 3209.

The BIR Library is open weekdays 9 a.m.-5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (excepting the historical collection) are available on loan.

Product News

METASTRON™ IN ADVANCED PROSTATIC CANCER

Metastron is a unique form of therapy, given as an outpatient injection. Following administration, Metastron localizes at the sites of metastases within bone, where it can provide relief of pain in 75% of patients. The average duration of relief is 6 months. The only known adverse effect is a depression of platelets that is seldom clinically significant. The patient will not experience nausea or vomiting.

The main advantages of Metastron over conventional radiotherapy are the selective uptake and retention by tumour sites in the bone. Thus, Metastron is able to irradiate multiple lesions simultaneously, with selective sparing of other tissues.

Metastron has an important place in the treatment of patients suffering from bone pain secondary to prostatic cancer, who are no longer responsive to hormonal manipulation. The majority of patients can expect pain relief from a single injection for an average of 6 months' duration.

For further information contact: Amersham Healthcare, Amersham Place, Little Chalfont, Bucks HP7 9NA.

GUY'S/LEWISHAM RADIOLOGY SYSTEM

The Guy's and Lewisham Hospitals Trust has commissioned a new computer system for its Diagnostic Imaging Departments. Stalis Consultants have developed the new system, among the many features are: patient index linked to the PAS index; patient registration and attendance recording; film reporting with word processor links; clinical coding; Korner statistics and Working Paper 11 outputs. The Trust intends to market the system within the NHS, with support services available from Stalis Consultants. The cost of purchase should be less than comparable commercial packages.

For more information contact: Dr C Bradshaw, Consultant Radiologist, Lewisham Hospital, Tel: 081-690 8947.

Xpeed and Xpress: State of the Art CT-Scanners

Toshiba Medical Systems Europe has introduced two new CT scanners, the Xpeed and the Xpress.

The Xpeed provides a CT-scanner that makes quick work of complex procedures; with a 2 MHU tube and a scan time of merely 1.6 seconds, it fulfils the highest demands, pampering even the most experienced operators. Simple icons, e.g. for magnification, gantry tilt, couch positioning and image processing functions, eliminate complicated operator intervention. The touch panel means that every conceivable procedure can be performed at the touch of the plasma screen. A "voicelink" allows pre-programming of up to 32 customized patient messages.

PMC (Patient Movement Correction) has been introduced to reduce artefacts, a feature especially appreciated in abdominal scanning.

The Xpress gives a full, 380 degree scan in a mere 1.5 seconds, giving more

information in less time and at a lower cost than comparable systems on the market. Due to its continuous rotation, the Xpress scans up to 20 slices in 30 seconds in dynamic mode. With its resolution — 0.35 mm — Xpress can uncover minute anatomy and pathology.

The Xpress incorporates a UNIX based CPU. Our unique FACT (Fully Automatic CT) allows scanning by just one keystroke.

An Xpress couch and its table stroke of 185 cm, combined with a Gantry aperture of 72 cm, assures both patient comfort and ease of operation, for example for biopsies and other interventional procedures.

For more information contact: Toshiba Medical Systems Europe BV, Ms A. Bromberg, SP/PR department, Schieweg 1, 2627 AN Delft, The Netherlands. Tel: +31-15-610121. Fax: +31-15-622359.



Toshiba's CT-Scanner Xpress

OMT WINS QUEEN'S AWARD

Oxford Magnet Technology Ltd (OMT), a Siemens joint-venture company based in Eynsham near Oxford, has won a 1991 Queen's Award for Technological Achievement. John Woodgate, OMT's managing director is justifiably proud of his team's performance: "This award reflects the advances we have made in the

development of actively-shielded, superconducting magnets for use in human body MRI systems", he said. OMT is the world's largest manufacturer of magnets for MRI.

For more information contact: David Sanders. Tel: 0932-752321. Fax: 0932-752337. Siemens plc, Siemens House, Windmill Road, Sunbury-on-Thames, Middlesex, TW16 7HS.

US Universities Order New Varian Products

Two Californian academic health centres have taken delivery of Varian Medical Equipment's new Clinac 2300C/D radio-therapy linear accelerator.

Stanford University Hospital plans to use the new dynamic conformal therapy accelerator for therapy and research. Conformal therapy is the technique of optimally shaping a beam of radiation produced by a linear accelerator to the patient's tumour volume while sparing healthy surrounding tissue. The University of California Irvine (UCI) Medical Centre will be the first cancer treatment centre to make its Clinac 2300C/D operational in January 1992.

There are two immediate clinical uses for the Clinac 2300C/D: total body irradiation for bone marrow transplantation and treatment of lymphoma patients. Stanford also has the Multileaf Collimator, a device for contouring the radiation beam, and PortalVision Electronic Portal Imaging for real-time verification of X-ray beam placement. Major studies to be undertaken at UCI include research in conformal therapy, the physics of beam dynamics, and patient treatment for national clinical trial investigations.

For more information contact: Christine Oliver, Varian Medical Equipment, Building 5B, 3045 Hanover Street, Palo Alto, CA 94303 USA. Tel: +415-424-5033.



The Clinac 2300C/D is the latest addition to Varian's C-Series

THREE NORTH EAST ULTRASOUND INSTALLATIONS COMPLETED BY KONTRON

Kontron Instruments has installed three ultrasound imaging systems at hospitals in the North East. The Queen Elizabeth Hospital in Gateshead has purchased a Kontron Sigma 1 Star Ultrasound scanner for its Special Care Baby Unit. This is being used for ultrasound examination of neonatal heads and abdomens and for various cardiac investigations. The same system has also been purchased by Sunderland District General Hospital for its Neonatal Unit. Darlington Royal Memorial Hospital are using a Kontron Sigma 1

Sector Linear System as a portable machine in the main Ultrasound Department. The equipment will be used with 3.56 and 5.00 MHz transducers for abdominal scanning of patients.

Medical staff are impressed by the clear image quality provided by the Sigma range which permits diagnosis even in difficult clinical areas.

For further information contact: Drew Mowatt, Kontron Instruments Ltd, Blackmoor Lane, Croxley Centre, Watford, Herts WD1 8XQ. Tel: 0923 56252.

High-definition™ imaging for the Ultramark 9 ultrasound system

Advanced Technology Laboratories, Inc. (ATL) have introduced High Definition Imaging. The HDI™ option offers a major advance in ultrasound image quality and pulsed and colour Doppler sensitivity. Building on the platform of the Ultramark 9 system, a new level of detail, tissue differentiation and haemodynamic flow information is available. This makes it easier to detect subtle abnormalities.

The digital beamformer extends the frequency of transducers to ranges never before achieved. The new HDI scanheads contain up to 192 elements and large apertures for uniformly high resolution images, greater resolution at deeper depths and superb penetration. The L10-5 High Resolution Linear Array transducer has a frequency range of 5–10 MHz. This probe allows detailed evaluation of superficial structures and plaque morphology and it is expected to be the new standard for thyroid, breast, testicular, shoulder and superficial mass scanning. The wide bandwidths and large apertures of the HDI curved arrays provide high tissue resolution and uniformity. A new curved array intravaginal scanhead has a 160° field of view.

The HDI option is available on all new Ultramark 9 systems and as an upgrade for current system owners. ATL is continually enhancing the system's clinical value.

For more information contact: Mike Andrews, ATL UK Ltd, Arden Press House, Pixmore Avenue, Letchworth, Hertfordshire, SG6 1LH.



ATL's Ultramark 9 HDI Ultrasound system

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

AEA Technology

Wigshaw Lane, Culcheth
WA3 4NE. Tel. 0925-252000 Ext. 4206
Product areas 7, 8.
Contact Mr J. G. Tyror, Director of Safety.

Agfa-Gevaert Ltd

27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Areas 1.
Contact Miss Anne Sparrow.

American Medical Ltd

PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC

Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr C. M. T. Medley, Sales and Marketing Manager.

Bard Ltd

Forest House, Brighton Road, Crawley,
West Sussex RH11 9BP.
Tel. 0293 527888, ext. 2204.
Product area 2.
Contact Peter Dekkers, Product Manager.

British Nuclear Fuels plc

Room 525, Hinton House, Risley, Warrington,
Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd

92 Uxbridge Road, Harrow, Middlesex,
HA3 6BZ. Tel. 081-954 2366.
Product areas 3, 6.
Contact Mr D. Lewis, Sales Manager.

Calumet Coach Co.

33 Shallbourne Rise, Camberley GU11
2EJ. Tel. 0276 64490.
Product areas: 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd

95A Finaghy Road, South Belfast
BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown, Managing Director.

Cea (UK) Ltd

25 Presley Way, Crownhill,
Milton Keynes MK8 0ES
Tel. 0908 263090. Fax: 0908 263546.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Clinical Press Ltd

Redland Green Farm, Redland, Bristol BS8
7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Computer General

5 Greenway Business Park, Bellinger
Close, Chippenham, Wiltshire SN15 1BN.
Tel. 0249 445566. Fax. 0249 445595.
Product areas 1, 10.
Contact Alan Mawdsely, Division Manager/Yvonne Morris, Marketing Manager

Data-Med Computer Services Ltd

10 Faraday Building, Highfields Science
Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fildes, Sales Manager.

Du Pont (UK) Ltd

Wedgwood Way, Stevenage, Hertfordshire
SG1 4QN.
Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager,
Diagnostic Imaging.

E. G. & G. Limited

Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive (Therapy).

Elsint (GB) Ltd

Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT. Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd

1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd

125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd

34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Mr Brian Scott, Commercial Manager.

IGE Medical Systems Ltd

352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd

PO Box 66, Station Road, Hemel
Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
Product area 1, 3, 4, 6, 8, 9, 12, 13, 14, 15
Contact Mr J. J. G. Tweed, Manager,
Health Sciences Division.

Lanmark

PO Box 317, Beaconsfield, Bucks
HP9 2LR. Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC

3M House, Bracknell, PO Box 1,
Berks RG12 1JU. Tel. 0344 858000.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd

11 North Portway Close, Round Spinney,
Northampton NN34RQ. Tel. 0604-646132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Man-
ager.

M.A.S. Medical Ltd

Armytage Road, Brighouse, West York-
shire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing
Director.

Meadox (UK) Ltd

Matthew House, Matthew Street,
Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and
Marketing Manager.

Medical Xray Supplies Ltd

Unit 12, Kingsbury Industrial Estate,
Church Lane, Kingsbury, London
NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr
K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd

Travellers Lane, Hatfield, Herts AL108XB.
Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and
Marketing Manager.

Nuclear Associates

100 Voice Road, Carle Place, New York
11514-1593, USA. Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd

Nucletron House, Tarporley Business
Centre, Tarporley, Cheshire, CW6 9UY.
Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office
Manager.

Nycomed (UK) Ltd

Nycomed House, 2111 Coventry Road,
Sheldon, Birmingham B26 3EA.
Tel. 021-742 2444.
Product areas 1, 3.
Contact Mr L. Birch Hansen, Managing
Director.

Oxford Magnet Technology

Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales
and Marketing.

Philips Medical Systems

Kelvin House, 63-75 Glenthorne Road,
Hammersmith, London W6 0LJ.
Tel. 081-741 1666.
Product areas 1, 2, 3, 4, 6, 9.
Contact Mr R. Van der Ploeg, Marketing
Manager.

Premise Engineering Ltd

Tibbs Hill Road, Abbots Langley,
Watford, Herts WD5 ODR.
Tel. 0923-267433/263320.
Product area 8.
Contact Mr R. K. Beach, Director.

Quantel Ltd

Administration Centre, Kiln Road,
Newbury, Berkshire RG13 2HA.
Tel. 0444 232323.
Product areas 2, 10.
Contact Mr Christopher Trim, Publicity
Officer.

Radiological Protection Services Ltd

61 Lind Road, Sutton, Surrey SM1 4PP.
Tel. 081-643 6374.
Product area 8.
Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd

The Brow, Burgess Hill, West Sussex
RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or
Mr S. Hearne, Product Managers.

Siemens plc

Siemens House, Windmill Road, Sunbury
on Thames, Middlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing
Assistant.

Sony (UK) Ltd

Jays Close, Viabes, Basingstoke, Hants
RG22 4SB. Tel. 0256 483564.
Product area 14.
Contact Richard Holt, Marketing
Manager.

Toshiba Medical Systems UK

Manor Court, Manor Royal, Crawley, West
Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray
Products.

Toshiba Medical Systems Europe BV

Schieweg 1, 2627 An Delft, The Neth-
erlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P. Blonk, Office Manager,
X-ray BU.

Vertec Scientific Ltd

5 Comet House, Calleva Park Estate,
Aldermaston, Reading RG7 4QW.
Contact Mr Frans Verlaan, Managing
Director

Wardray Products Ltd

Hampton Court Estate, Summer Road,
Thames Ditton, Surrey KT7 0SP.
Tel. 081-398 9911.
Product area 8.
Contact Mr R. B. Wardley, Managing
Director.

William Cook (Eur) Ltd

6 Such Close, Letchworth, Hertfordshire
SG6 1JF. Tel. 0462 482884 Fax: 0462 480944.
Product area 2.
Contact Tessa Phizacklea, Product
Manager.

X-rite (H. Miller Graphics Ltd)

8 Moody Street, Congleton, Cheshire
CW12 4AP. Tel. 0260 279988.
Product areas 1, 12.
Contact Mrs P. Dhanani, Medical Sales.

KEY TO PRODUCT/SERVICE AREAS

- | | |
|--|--|
| 1: Diagnostic X-ray including NMR and CT | 10: Image processing |
| 2: Interventional radiology | 11: Nuclear fuel cycle services |
| 3: Ultrasound | 12: Quality assurance. |
| 4: Nuclear medicine | 13. Radiology data management computer systems |
| 5: Radiopharmaceuticals | 14. Video printing |
| 6: Radiotherapy and oncology | 15. Equipment leasing |
| 7: Radiobiology | 16. Hospital-shared services |
| 8: Radiation protection | 17. Medical Publishing |
| 9: PACS | |

Meetings and Courses

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR

The Role of Technical Standards in Marketing Medical Devices in Europe

September 12-13, 1991

Brussels, Belgium

Further details: Charlotte Thornton, IBC Ltd, Bath House - 3rd Floor, 56 Holborn Viaduct, London EC1A 2EX
Tel: 071-236 4080 Fax: 071-489 0849

European Congress of Radiology '91

September 15-20, 1991

Vienna, Austria

Further details: The Congress Secretariat ECR '91, c/o Vienna Academy of Postgraduate Medical Education and Research, Alser Straße 4, A-1090 Vienna, Austria
Tel: (1) 421383 Fax: (1) 42138323

Second International Congress on Ultrasound and the Skin

September 18-21, 1991

Modena, Italy

Further details: Stefania Seidenari, Dept. of Dermatology, Policlinico - via del Pozzo, 71 41100 Modena, Italy
Deadline for abstracts: June 15 1991

Second International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation and Radiation Injury

September 18-21, 1991

Berlin, West Germany

Further details: Dr Santosh Nigam, Local Organizing Secretariat, Eicosanoid Research, Dept. of Gynecological Endocrinology, Universitätsklinikum Steglitz, Free University Berlin, Hindenburgdamm 30, D-1000 Berlin 45, Federal Republic of Germany

Lipid Lowering Agents - A Critical Review

September 23-24, 1991

London

Further details: Georgina Mason, IBC Technical Services Ltd, Bath House, 3rd Floor, 56 Holborn Viaduct, London EC1A 2EX
Tel: 071-236 4080 Fax: 071-489 0849

INMEDTEC '91

September 24-October 1, 1991

Kiev, USSR

Further details: Nowea International GmbH, Postfach 320203, Stockumer Kirchstraße 61, D-4000 Düsseldorf 30, Germany.
Tel: (0211) 456002 Fax: (0211) 4560740

Diagnosis of Musculoskeletal Disorders: State of the Art

September 25-28, 1991

California, USA

Further details: Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, Georgia 30077-1925, USA
Tel: (404) 641-9773 Fax: (404) 552-9859

Dublin 91: Annual Scientific Meeting and Exhibition

September 25-28, 1991

Dublin, Ireland

Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG
Tel: 071-636 4432 Fax: 071-323 3100

XIIIth International Congress of Lymphology

September 29-October 5, 1991

Paris, France

Further details: Medical Congress Management, PO Box 2, CH-8029, Zurich, Switzerland
Tel: (01) 255 19 15 Fax: (01) 261 05 78

BIOBURDEN Workshop

September 30-October 1, 1991

Frankfurt, Germany

Further details: Charlotte Thornton, IBC Ltd, Bath House - 3rd Floor, 56 Holborn Viaduct, London EC1A 2EX
Tel: 071-236 4080 Fax: 071-489 0849

Practical Implications of ICRP 1991

October 1, 1991

London

Further details: Dr D. N. S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian, EH49 6AS
Tel: 031 - 244 2779

Current Concepts of Magnetic Resonance Imaging

October 3-6, 1991

California, USA

Further details: Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, Georgia 30077-1925, USA
Tel: (404) 641-9773 Fax: (404) 552-9859

XIIIth International Congress of Head and Neck Radiology

October 6-9, 1991

Zurich, Switzerland

Further details: Medical Congress Management, PO Box 2, CH-8029, Zurich, Switzerland
Tel: (01) 255 19 15 Fax: (01) 261 05 78

Multi-Disciplinary Up-Date Course (Triple Assessment)

October 7, 1991

Nottingham

Further details: Mrs B Price, Training Coordinator, Nottingham Breast Screening Training Centre, City Hospital, Hucknall Road, Nottingham, NG5 1PB
Tel: 0602-691689 Fax: 0602-627707

MR Update: Neuroradiology and Musculoskeletal Radiology

October 7-12, 1991

South Carolina, USA

Further details: Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, Georgia 30077-1925, USA
Tel: (404) 641-9773 Fax: (404) 552-9859

XVIIIth Congress of the European Society of Neuroradiology

October 8-12, 1991

Zurich, Switzerland

Further details: Medical Congress Management, PO Box 2, CH-8029, Zurich, Switzerland
Tel: (01) 255 19 15 Fax: (01) 261 05 78

Advances in Molecular Research

October 9-12, 1991

Garmisch-Partenkirchen, Germany

Further details: Georgina Mason, IBC Technical Services Ltd, Bath House, 56 Holborn Viaduct, London EC1A 2EX
Tel: 071-236 4080 Fax: 071-489 0849

How to Detect and to Characterise the Microcalcifications?

October 10, 1991

France

Further details: M J Rodiere, Institut D'Imagerie Medicale, Miniparc - Bat 2, Rue de la Croix Verte, 34090 Montpellier, France

Interventional Radiology Workshop

October 17-18, 1991

Hampshire

Further details: Kim Bailey, Educational Support Administrator, Meadox (UK) Limited, Matthew House, Matthew Street, Dunstable, Beds. LU6 1SD
Tel: 0582-605111 Fax: 0582-699406

6th Bristol Cardiac Ultrasound Course

November 18-21, 1991

Bristol

Further details: Dr Duncan Ettles, Dept. of Radiodiagnosis, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW
Tel: 0272-739746

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.